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EDITORIAL

CARCINOMA OF THE TONGUE

THE JOURNAL has been very fortunate in obtaining for this issue a paper by a noted Toronto graduate on the Treatment of Carcinoma of the Tongue. In the comparatively few years that have elapsed since his graduation, Dr. Douglas Quick has made a very high name for himself, and done great honour to his Alma Mater. He early became actively associated with the development of the radiation treatment of malignancy, and being in the rather unique position of expert radiologist and surgeon, was not embroiled in any controversies about methods of treatment, but wisely realized the possibilities afforded by an intelligent and scientific co-operation of the two. His skill and energy rapidly brought him to the position of Attending Surgeon to the Memorial Hospital, New York City.

In this institution research and treatment have been elevated to a very high plane. The patients are largely cancerous. The hospital is famed for its remarkable success in treating these previously so fatal cases. In carcinoma of the mouth and tongue particularly, it is universally acknowledged to have a much higher proportion of cures than has ever yet been attained elsewhere.

Dr. Quick addressed the Academy of Medicine here last year, and was signally honoured in being invited to present his results before the International Congress in London during the past summer. He has very kindly prepared for the JOURNAL an article embodying the main features of the latter address.

"NOTES FOR DIABETICS"

IT is a well recognized fact that an adequate diet is the most important factor in the treatment of diabetes. Recent, rapid advances in the principles of dietetic treatment of this disease now fortunately render it a comparatively simple matter for anyone to undertake intelligent treatment. Clinical teaching and various papers that have appeared from time to time in this and the Canadian Medical Association Journal clearly indicate the methods that are being so successfully employed in the Toronto General Hospital.

Only the practitioner who has endeavoured to so treat a case oustide of hospital, and without the aid of a trained dietitian, can realize the labour involved in translating a simple dietary prescription into a daily menu for his patient. Treatment frequently fails solely on account of the monotony of the necessarily neglected nature of the patient's diet. Monotony is not a necessary accompaniment of a diabetic diet, and such failures should not occur. The solution of the difficulty rests with the patient himself. Numerous handbooks now on the market endeavour to instruct him in following out his doctor's dietary prescription by enumerating type diets and presenting elaborate tables of foodstuff analyses. Most patients, however, have neither the training nor the time to use the common dietary dodges; and anyone who has tried to achieve variety from such tables will agree that it is a very difficult matter.

In consequence of this we welcome the appearance in "Notes for Diabetics" of the material long used in mimeographed form by Dr. W. R. Campbell and Miss Mame Porter for the instruction of their patients. The "Notes" explain to the patient certain facts about diabetes and its dietetic control, which are essential foundations for his intelligent co-operation with his physician, and also provide him with a number of tested recipes for suitable foods. Instruction is given in the construction of menus from a dietetic prescription.

The distinctive and invaluable feature of the book is the insertion of a much needed chapter of "Tables of Equivalents" for eggs, bacon, beef, custard, and those other constant and frequently detested constituents of the typical diabetic diet. Dr. Campbell does not worry the tyro with percentage tables, but simply suggests a list of the quantities of numerous foodstuffs, which, by the simple addition or subtraction of a measured amount of butter, may be substituted in the diet for the common quantities of any of the components of the standard diabetic diets. For the patient who has received preliminary instruction, complete analytical tables are presented in a later chapter.

We feel confident in stating that all diabetics and their physicians will heartily welcome these "Notes," and that anyone starting in to treat a diabetic without insisting on his acquisition and utilization of the book, is not aware of the difficulties that lie before him in his seemingly simple task, and of the frequent failures that ensue from no other cause than that old and needless curse of monotony in the diabetic diet.

TETANUS

NO apology is necessary for a consideration of this subject to those who have had even a meagre experience at any large, receiving city hospital. Here, almost invariably, the case that comes in diagnosed tetanus has come because someone has failed to use the available prophylactic measures—because someone has forgotten. But still more regretful, so little is now left to be done, as the case has progressed too far. The stigma of such a case need never haunt any practitioner of medicine. It is the infrequency of the case which allows us to forget, and which permits of our being repeatedly reminded of its dangers.

The existence of anti-tetanic serum makes tetanus 100 per cent. preventable. Prophylaxis is the one sure method of treatment. Does the giving of prophylactic doses of anti-tetanic serum offer any danger of anaphylactic shock? This doubt is quickly disposed of by the record that of two million prophylactic injections of tetanus anti-toxin administered in the British Army during the war, only eleven cases of shock occurred, and all of these recovered. As in the giving of other serums, one must consider each case on its own, being particularly careful in an asthmatic subject and the related chronic chest conditions. The subcutaneous desensitizing dose can always avoid this complication.

What, then, are to be the prophylactic methods, and when are they to be adopted?

It is well known that the Bacillus of Tetanus thrives best under anaerobic conditions in lacerated tissues which are deprived of their blood supply. In treating such we should then aim to remove all devitalized tissue, and in doing so to avoid such methods as the cautery or the use of antiseptics, such as carbolic acid, which will produce further death of tissue. The deep puncture wound should, where feasible, be laid open, swabbed with tincture of iodine, and covered with dry sterile dressing. Particularly does this apply to the lower extremity and to those small penetrating wounds in children due to exploding powder. Immediately the wound is dressed, anti-tetanic serum is indicated. The dose is usually 1500 units, given intra-muscularly (after subcutaneous desensitization), the site of choice being well above the gluteal fold of the buttock. This dose is sufficient to protect against 2000 times the minimal fatal dose of toxin.

This accounts for the simple case of prophylaxis; but there are some conditions which may even escape the careful man. These are the persistently discharging sinuses following upon puncture wounds or compound fractures. The protective action of a prophylactic dose of anti-toxin persists for about ten days, so that a patient with the above condition should have repeated doses at this interval, and whenever repeated manipulation of a compound fracture is necessary. From a great host of records the average incubation period in the unprotected cases has been found to be ten days. The mortality is known to be directly proportional to the shortness of the incubation period. Since British war statistics (in treated cases which have received a minimal

dose of 500 units and have ultimately developed tetanus) show the average incubation period as 45 days, one can comprehend the value of prophylaxis in any case where one is the least dubious.

But what of those cases where no prophylaxis has been used and in which symptoms are already present. Trismus or spasm of the muscles of the jaw, known to the laity as "lock-jaw," is possibly the most important symptom—which, together with neck rigidity, make the diagnosis fairly certain. These cases which we are called upon to see with symptoms already well defined must be treated with dogged persistence until a cure or death occurs.

The therapeutic aim now is to neutralize the tetanus toxin before it becomes permanently fixed in the ganglion cells. Controversy as to the path of travel of the toxin within the body, whether by way of the axis cylinder or by lymphatics, has been fairly definitely settled in favour of the latter route. The treatment is based on this view. The prime indication for treatment, then, is to maintain as high a concentration of anti-toxin as possible in the blood and lymph stream.

Sherrington's work in comparing the relative efficiency of different routes of injection of serum reports the lowest mortality with intrathecal injections. This route should not be omitted even when the patient has developed a marked opisthotonus. In these cases a general anaesthetic should be given, and lumber punctures can then be done, cerebro-spinal fluid removed and serum injected by gravity at body temperature. The subcutaneous, intramuscular and intravenous routes and interstitial injection of serum about the old wound should be employed concurrently.

A review of the literature would warrant a total initial dose (by way of the various routes) of 50,000 units, which on the second day can be increased to 75,000 units, and this dose continued daily until the disease is controlled. The dose for a child should not be much less than for an adult, as the child has the same amount of toxin to neutralize.

Fluids given by whatever route should not be neglected. The most efficient sedative for these cases is a subcutaneus injection of a 5 per cent. solution of chemically pure magnesium sulphate, given in small doses of 10 to 15 cc. four or five times daily as the case demands. This same strength solution may be safely used intravenously. The other common sedatives may be used singly and with caution.

Before the introduction of serum the death rate from tetanus was 85 per cent. The British war records of over 2,000 active cases treated report a mortality of 47 per cent. This figure could no doubt be greatly reduced in practice with better nursing facilities and larger available supplies of anti-toxin.

THE TREATMENT OF TUBERCULOUS ABSCESS AND SINUS*

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The tuberculous abscess, so frequently associated with tuberculous disease of bones and joints, is usually looked upon as a mere adjunct or complication of a serious condition, and its treatment therefore is not considered carefully. As a matter of fact the abscess should be treated as the gravest element in the disease, because it is from this source for the most part that other organisms are introduced, and the added infection is the cause of the largest percentage of the mortality in this disease. The tubercle bacillus is now looked upon as an organism of low virulence for the bulk of people with an average resistance, but as soon as the disease has added another infective organism, the outlook is changed and the mortality is tremendously increased. It is a fair estimate that well over ninety per cent. of all cases with pure tuberculous infection of bones or joints get well, with greater or less loss of function. It is equally true that a very large percentage of the cases with mixed infections do not recover. The mortality from the pure tuberculous infection is mostly from invasion of other tissues, usually the central nervous system or kidneys, whereas the cases with mixed infections die of amyloid disease of the abdominal viscera or from exhaustion from long continued suppuration.

In a paper before the American Orthopedic Association in 1901 the writer made the statement that no case of amyloid disease had ever been seen with a simple tuberculous infection, and at that time it was a common condition due to the prevalence of mixed infection from faulty methods of dealing with tuberculous abscesses. From a wide experience since that time the statement has been proven true, and now in a very large clinic it is quite rare to find amyloid disease, due undoubtedly to the fact that every precaution is exercised to prevent mixed infections.

In most text-books at the present time very scant instructions are given as to the method of caring for tuberculous abscesses, and the dangers of mixed infections are nowhere emphasized sufficiently. The method of dealing with septic abscesses, on the other hand, is adequately stressed, and the average young practitioner makes the mistake of treating both alike, with very serious detriment to the tuberculous case. In 1890 Mr. Watson Cheyne recommended the complete excision of the abscess in tuberculous bone disease. This would be an ideal method if it were generally applicable. Unfortunately its use is very limited and has never been considered of real value in dealing with the problem in a large way.

Expectant Treatment.—It is urged that the abscess is an extension from a primary bone focus, and as the disease is progressive the abscess will recur if the contents are removed. This is only partially true. The abscess develops by the caseation and liquefaction of a tuberculous focus in bone, and as the degenerative process spreads in the bone this liquefied material breaks through and extends into the soft tissues. It

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extends in the line of least resistance and is known to do so for great distances from the primary focus. As it continues to enlarge, almost the entire contents are broken down debris of bone and invaded soft tissues, and the wall is a granulation wall, the so-called "pyogenic membrane" of earlier writers. This granulation wall varies in thickness, but in it is found the active tuberculous process. Numerous pathological tubercles can be demonstrated and here the tubercle bacilli are found abundantly. The liquid contents of the abscess contain in many instances no bacilli, or at any rate very few. The expectant treatment is really a patient waiting to observe the progress of the abscess under careful and efficient treatment which is especially directed to the treatment of the local focus. In a fairly large number of cases the abscess will recede rather than progress under these circumstances.

In the mind of the writer the efficient treatment of the local condition means recumbency with protection from movement as largely as possible, and entire protection from weight bearing during the active stage. This means twelve to eighteen months on a frame or splint in the case of the spine or hip disease, and a correspondingly shorter period in the case of the knee or smaller joints. The general treatment of the patient consists in careful and abundant nourishment of an easily assimilated kind, with a free administration of fruits and green vegetables, good hygienic surroundings, and heliotherapy. Even in a rigorous climate exposure of the patient to the sun's rays after the plan of Rollier can be carried out for at least six months of the year, and the mercury quartz lamp is found to be a useful adjunct during the extreme winter months. If the abscess progresses steadily in spite of careful treatment, and gradually works closer to the surface, it is questionable whether it should be left alone longer. If left, it will gradually invade the skin, and this tissue will become tuberculous and the abscess may become infected with skin organisms, chiefly staphylococci, from the sweat glands which harbour them. The granulation layer formed on the under surface is undoubtedly a partial safeguard, and the skin may break through and the abscess contents be discharged without mixed infection of the cavity.

Aspiration.—If it is decided that in such a progressive abscess interference is necessary aspiration is often considered the safest means of treatment. There are several difficulties which will be encountered. First, the contents of nearly all such abscesses contain, in addition to the "whey" or definitely liquid portion, a fairly large proportion of "curd" or semi-solid debris which will not pass through even a very large bore aspirator. Hence it is found that repeated attempts at aspiration fail because of plugging of the aspirator needle. Again, even if partially successful, and the tension of the abscess is relieved at least for a time, there is a real danger from withdrawal of the needle that tuberculous material will be lodged in the track and a real tuberculous sinus result. This is frequently the case if the needle is plunged into the abscess in its most prominent and usually thinnest part; it is sometimes prevented by introducing the needle obliquely from a distance, penetrating a fairly thick section of skin and muscle tissue before reaching the abscess cavity. There is also a further difficulty in the location of some of the abscesses, and it often entails a degree of courage bordering on foolhardiness to attempt to aspirate a psoas abscess under certain conditions. After all these factors have been considered, however,

there is no doubt that a certain few cases of abscess may be treated successfully in this manner.

Aspiration and Injection of Antiseptics.—In the view of the writer, the added injection of any antiseptics after partial aspiration of an abscess is of very doubtful value theoretically. It does not sound reasonable to expect any effect on the protected organisms of the granulation wall of an abscess cavity when antiseptics are injected into, and diluted by, the fluid contents of such an abscess. In some clinics the injection of naphthol or of iodoform and glycerine has been used extensively, and the results, on the whole, are not as good as by the expectant method. Iodoform has been demonstrated of very little value in local applications to tuberculous processes, and when glycerine is added it destroys what little value the iodoform possessed. Since the glycerine is hygroscopic, serum rapidly fills the cavity which was partially evacuated by aspiration, and the danger of sinus formation along the track of the needle is increased. It is our opinion, therefore, that the injection method has no place in the treatment of these abscesses.

Incision.—It is so easy for the practitioner to fall into the error of thinking that tuberculous abscesses should be dealt with by the recognized method of treatment of "septic" abscesses, that is, they should be opened at as early a date as possible, and so as to ensure efficient drainage in the most dependent part. This method of early incision and dependent drainage, particularly when a rubber tube or similar drainage method is used, is in the great majority of cases the most likely to lead to disastrous results. Unless the incision is made under the strictest aseptic precautions and the drainage material removed within forty-eight hours, secondary infection is almost sure to supervene.

Incision with Closure of the Wound.—While the writer was serving an eighteen months' interneship in one of the New York Hospitals he was impressed with the very large percentage of cases with tuberculous abscess which became secondarily infected, and the dreadful emaciation and gradual exhaustion which followed. Amyloid changes in the abdominal viscera were also of frequent occurrence. A visit during the next year to many European clinics further impressed this fact, as similar conditions were found there. In 1901, at the American Orthopedic Association, the writer presented a short paper on the treatment of tuberculous abscesses by incision, cleaning out the granulation wall, and closure. The paper was based on thirty cases so treated, with primary healing in over ninety per cent. of cases and no secondary infections. This paper created a good deal of criticism, and showed that the older members especially had become so accustomed to the then existing condition that they accepted it as a matter of course. In 1907, at the meeting of the British Medical Association in Toronto, a further report was made of cases treated up to that time with similar findings. After an experience of about twenty-five years as a member of the Staff, and for many years as Surgeon-in-Chief of the Hospital for Sick Children in Toronto, the writer looks back with some pride at the changed conditions in regard to tuberculous bone diseases, especially with regard to the very small number of cases of mixed infections. At the present time it is rare to find a case of mixed infection in this clinic, and amyloid disease is practically unknown. With this change it is

also noted that very few cases of tuberculous meningitis are found following bone tuberculosis.

The routine technique followed for many years with regard to tuberculous abscess is to follow the case expectantly, treating the bone lesion and carefully watching the abscess. In a fairly large and gradually increasing proportion of cases the abscess subsides, and in process of time becomes a thickened or calcified mass in the region where the abscess was present. The X-ray will often verify these findings. As in tuberculous tissues anywhere in the body the cure of the lesion is by a substitution of fibrous tissue or calcareous deposits, it is assumed that in the case of the abscess a real cure has resulted.

Surgical interference is advised in the cases where, in spite of careful treatment of the original bone lesion, the abscess gradually increases in size and ultimately threatens to invade the skin. After careful preliminary preparation of the skin an incision is made large enough to explore the cavity thoroughly. This incision is made in the least dependent area and through healthy tissues, often at quite a distance from the abscess cavity, so as to insure a thick layer of muscular tissue between the abscess cavity and the skin, and to prevent the filtering down of any remaining tuberculous organisms by gravity into the line of the incision which would result in a tuberculous track or sinus. As soon as the cavity is opened a "sucker" is inserted and the contents aspirated to prevent soiling of the wound as far as possible. The cavity is then opened widely, carefully retracted, and the entire granulation wall cleaned out with gauze sponges or iodoform gauze. The bleeding is controlled by pressure and the entire cavity is swabbed out with 2½% iodine. The incision is then thoroughly mopped with alcohol to clear out any debris and the deep structures brought together with interrupted catgut sutures. The fascia is closed with continuous catgut suture and the skin closed with horsehair. Pressure is maintained where possible during closure of the wound, to prevent filling with serum, and a heavy pad or dressing applied with an elastic flannel bandage. The great majority of these wounds heal by primary union. In a few instances a second operation is found necessary, and in a few cases aspiration is resorted to if the cavity rapidly fills up and endangers the suture line. In most cases there is a moderate refilling of the cavity with serum, but this is soon absorbed. After these many years of experience it has not been found that this radical cleaning out results in spread of tuberculous disease to other distant tissues.

This method has been practised in many other clinics since first advocated by the writer, and in some the results have not been nearly so satisfactory as in our own clinic. Investigation has shown that the fault has been for the most part due to careless technique, particularly in the failure to make the incision through as wide an area of healthy muscular tissue as possible, to place a wide barrier between the cavity and the skin surface. This method is still recommended as the method of choice in dealing with this troublesome complication.

Sinuses.—The treatment of tuberculous sinuses is still a matter of controversy. There are no doubt a large number of cases of abscesses treated expectantly, which ultimately rupture and discharge their contents and do not become infected. This is especially true in some of the institutions where heliotherapy is the chief or sole method of

treatment of tuberculous disease. It was the writer's privilege a short time ago to visit such an institution, and it was rather a surprise to see so many cases with sinus, and apparently none of them more than superficially infected. The method adopted for treatment of these conditions in our clinic is first to absolutely prohibit any medical officer or nurse to put anything into the sinus; no probe or drainage tube or attempt at irrigation or swabbing of the sinus is permitted. In the second place, dressings are done as infrequently as possible and at the same time keeping the area clean. When dressings are done the surface is wiped off with alcohol and a fresh dressing applied, preferably of some antiseptic gauze such as the double cyanide of mercury and zinc.

After a fair trial of many methods of dealing with such sinuses, as irrigation with saline, Dakin's solution, swabbing with zinc chloride or carbolic acid, these have all been abandoned, and the treatment as above noted has proven the most efficient. In the cases where mixed infection has occurred, adequate dependent drainage is essential, and in superficial lesions such as are found in the extremities, many of these can be cleared up in time. In the psoas abscesses with mixed infection, however, the writer has become definitely pessimistic. The difficulties of adequate drainage are so great that very few of them will recover, and the mortality is greatest among these cases.

THE TREATMENT OF CARCINOMA OF THE TONGUE

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Carcinoma of the tongue, in spite of its relative accessibility, terminates fatally in 75-90 per cent. of cases. A very extensive study of the literature shows that surgical treatment of cancer of the tongue is apparently successful in 15-20 per cent. of the operable cases. However, a large percentage of patients are inoperable when first seen, either because of the extent of the lesion or weakened physical condition. Some refuse operation because of fear of surgery.

It was in the hope of improving these results that we took up the use of radium and X-rays. Our early experiences were not particularly encouraging; the cases were very advanced; dosage was inaccurate; we were using crude surface applicators and had very little knowledge of screening. Some favorable effect was produced, however, over the accessible portions of the growths with some tendency towards surface healing, and diminution of local infection. Histologically, we noted degeneration of tumor-cells, production of new connective-tissue, and marked infiltration of lymphocytes and plasma-cells in and about the growth.

Early in 1916, the late Dr. H. H. Janeway adopted an entirely new method of radium application in these tumors, *i.e.*, the introduction into the tissues of small glass capillary tubes containing radium emanation. Such a radical departure from previous methods was, of course,

accompanied by many errors; but in spite of this, our results improved, due probably to the accuracy and uniformity of application. These capillary glass tubes—or "bare tubes"—are approximately 3x0.3 mm. in size; tubes containing approximately 1 mc. of radium emanation represent the most satisfactory value. This emanation decreased in strength at an approximate rate of 15 per cent. per day, so that a calculation of total dosage derived from a 1 mc. tube shows about 132 mc. hours of radium energy, which, distributed over a period of at least a fortnight, offers a prolonged radiation and permits of greater total dosage.

In general, we plan to use a 1 mc. tube per cu. cm. of tumor tissue, when the tumor is spherical; an elongated lesion will obviously require more tubes for proper distribution than the same bulk of tumor tissue in more compact form. The tubes should always be introduced in greater dosage along the infiltrating base of the growth rather than at its central point. When possible, it is wiser to introduce the trocar needle, by means of which they are implanted, through healthy tissue about the base of the growth rather than directly through tumor tissue.

Treatment of the Primary Lesion. Just as cases were formerly classified as operable and inoperable, surgically, it is now necessary to classify them somewhat empirically, as favorable or unfavorable from a radium standpoint. In the group classed as favorable, which embraces a larger number of cases than may be considered surgically operable, treatment should be pushed to the limit. In addition to the use of physical agents, the most rigid oral hygiene must be instituted and followed throughout. Before implanting emanation in the growth, external radiation in the form of X-rays or radium packs should be applied. This preliminary external dose causes inhibition of growth, thus obviating the possibility of implanting tumor-cells in normal tissue beyond the base of the tumor, provided the needles have to be introduced through malignant tissue.

Following this initial external radiation we employ a single application of bare tubes to care for the entire lesion. A lesion requiring a subsequent dose to care for a part of the growth missed the first time is considered distinctly unfavorable; the second dose must be delayed several weeks; the patient's strength is often reduced; the tissues, because of reduced blood-supply, do not tolerate the second dose as well as the first; the danger of slough and haemorrhage is consequently greater.

Following the introduction of bare tubes there is a sharp inflammatory reaction which may be aggravated by mixed infection if it is not rigidly cared for. This reaction leaves the tongue swollen and painful for a period of 4-8 weeks. In many instances it results in slough, and at times haemorrhage following separation of the slough. The danger of breaking down of tissue is always increased by infection, but may be present without it, and represents the chief disadvantage of this method of radium application. If there is danger of extensive slough, the external carotid artery on the involved side, together with its lingual and facial branches, should be ligated under local anaesthesia. It is

this necrosis of tissue which has led to so much unfavorable comment on the method. The necrotic area, however, represents only a small portion of the entire area treated, and the maximum effect of radiation extends far beyond the slough. When the patient's general strength does not seem to warrant carrying through the entire period of inflammatory reaction the duration may be shortened by some form of local surgical removal of the condemned area. This leaves a clean, much less painful surface which heals more rapidly. For this we prefer a high frequency electric cautery. Some of the irregular scars resulting after separation of radium slough can be improved by the same method.

The only condition in which we favour surgery directly for the treatment of tongue cancer, is in a tongue, the seat of a generalized syphillitic glossitis. Here the amount of fibrous tissue present, and the consequent reduction in blood supply, result in such extensive necrosis from the use of radium that we prefer removal of the entire tongue after a preliminary external radiation, planning to meet recurrence promptly by the introduction of emanation over a smaller area. A tongue that is the seat of a syphillitic leukoplakia only, does not require surgical removal. It is quite another problem than the generalized glossitis. I doubt if there is any advantage in attempting to clean up a deeply excavated, foul, fungating lesion by any surgical procedure followed by radiation; much better to leave this type of case to palliative treatment only.

When it comes to palliative treatment bare tubes do not play any appreciable part. External radiation in its various forms offers more, with much less of suffering on the part of the patient.

For a long time we have been trying to obviate the painful destructive effects of the bare tubes, and recently Dr. Failla, Director of our Physical Department, has succeeded in substituting gold tubes in which to collect the emanation instead of the glass tubes previously employed. These gold tubes, in all respects, are similar to the bare tubes, excepting that they are very slightly larger, and have the advantage of removing practically all of the beta radiation. I have treated a number of cases with these tubes, and am highly gratified by the results obtained.

Treatment of the Cervical Nodes: In the treatment of the cervical nodes we have not followed the generally accepted practice of doing a routine block dissection in all cases. We prefer intensive radiation combined with surgery, the latter being employed only in those cases where definitely palpable operable nodes are present. We feel that the lymph nodes perform a conservative function up to a certain point, and represent one of nature's chief barriers to the progress of the disease. We believe that, with epidermoid carcinoma at least, metastatic extension is by embolism and not by direct permeation of the lymphatics. It has been our experience that we rarely find more than one, or possibly two, nodes invaded until late in the course of the disease. This tends very strongly to support the embolic theory. A considerable percentage of cases do not develop metastases in the neck at all, or only late in the natural course of the disease. This is especially true in elderly patients and in the papillary type of epidermoid carcinoma.

Our plan has been to subject every case, immediately upon admission to the service, to heavy external radiation over both sides of the neck. For this we originally favoured the use of heavily filtered radium; but due to the economic impossibility of doing this in all cases we resorted to the use of higher voltage X-rays. At the present time we strongly favour a combination of both. If the case has no evidence of invasion of the cervical nodes at the time of this preliminary radiation we keep it under careful routine observation and repeat the radiation again as soon as the skin will stand it. If a firm moveable node is present on admission, or appears subsequently, we add a radium pack to the X-radiation cycle, and, as soon as the skin reaction subsides, do a complete unilateral surgical dissection, followed by burying bare tubes of radium emanation in the surgical field at any suspicious points, particularly where the lymphatic channels are severed. The incision is then closed in the ordinary fashion. This method affords an excellent means of applying very heavy dosage at the points where it is most needed, and, in my opinion, is the only form of post-operative radiation which is of any value. If, upon admission, the case presents a fixed node—even though it be a small one—suggesting that the capsule has already been perforated by the disease, so that tumor tissue is invading surrounding structures, we rarely resort to a surgical dissection. As time goes on, I become more firmly convinced that once the disease has extended beyond the capsule of node, it is, strictly speaking, surgically inoperable, even though it may appear readily operable from a technical surgical standpoint; I believe it is wiser to leave this case either to external radiation alone, or, if not too large, to follow the external radiation by surgical exposure and direct implantation of bare tubes throughout the invaded area.

If the metastatic involvement is more extensive upon admission, external radiation alone is all that is considered.

Our dissections are all done under local anaesthesia, and unless the primary lesion has been entirely cleared up, we take advantage of the surgical exposure to ligate the external carotid vessel just above the superior thyroid branch. In addition, the lingual and facial vessels are ligated separately in order to further reduce the collateral circulation.

During the past year we have been more strongly impressed than before by the possibilities of external radiation in the neck. By a more intensive use of shorter wave length X-rays, and particularly by combining these with the gamma rays of radium, in the form of heavily filtered radium packs, we have succeeded in producing results which we had formerly thought impossible. From a purely clinical standpoint I am convinced that different wave lengths have different selective actions.

Histological study of the material removed at operation seems to confirm our clinical observations. Different types of tissue reactions are to be noted following heavy external radiation over the neck. The skin, of course, is not damaged as much, per given quantity of radiation by the shorter wave lengths, as by the longer wave lengths of lower voltage X-rays. Formerly, it has been rather generally accepted that radiation produced atrophic changes in the normal lymph nodes. Such is not the

case. There is no evidence in our material showing destructive changes in the normal lymph nodes. On the other hand, a very marked hyperplasia occurs with an increase in the number of lymphocytes and plasma-cells. It is undoubtedly this reaction which explains the real value of so-called prophylatic radiation and pre-operative radiation. This reaction of the lymphoid tissue is, as far as we know, nature's chief barrier against tumor cells. This stimulation of the protective defences indicates that the chief value of the physical agents lies in the indirect, rather than the direct, effect upon invading tumor tissue.

From our observations it would seem that X-rays, in the wave lengths which are now possible, have a more marked effect on the connective tissue structures than radium. Radium, on the other hand, exerts a more destructive effect on capillary blood-vessels. By combining these agents we produce a much more uniform and generalized reaction. We find in the metastatic lymph node a marked thickening of its capsule, which tends, of course, to prevent outward invasion. The central necrosis noted in the involved node is undoubtedly a vascular change, and is hastened by increasing the radium dosage. This is followed by a liquefaction necrosis of the metastatic focus in the node; proliferation of connective tissue gradually replaces this process.

The rapidity and extent of tumor cell degeneration bears a very definite ratio to the lymphocytic and plasma-cell infiltration. The plasma-cell infiltration seems of even greater importance than that of the lymphocytes. This gradual process of destruction of tumor tissue metastatic in the cervical nodes, and ultimate replacement by fibrous tissue, requires a period of many weeks. It strongly suggests, therefore, that where operation is to follow preliminary radiation, a longer, rather than shorter, interval should elapse between the two procedures.

Because of the fact that we had never seen complete destruction of metastatic involvement from external radiation alone, we have continued throughout, in the strictly operable cases, to follow our radiation by dissection. The favorable changes noted from increasing the amount and type of external radiation has led us, so far, to lengthen the interval between radiation and operation. I believe we are now justified in going a step further and leaving some of these cases for still longer periods before surgical intervention. I believe it is not too much to expect that with further histological study, and further experience in the adjustment of dosage, that we may yet be able to accomplish more by the aggressive use of the physical agents alone rather than by the combined method employed heretofore.

I know that some writers have definitely reported complete regression of epidermoid carcinoma, metastatic in cervical nodes, from external radiation alone. We have always questioned these results; first, because it is difficult at times to determine whether a node is definitely invaded or not—an inflammatory node may very readily be mistaken for a metastatic node; and, secondly, because the same technique in our own hands fell short of giving complete regression.

Our experience with carcinoma of the tongue during this eight year period—from January 1st, 1917, to December 31, 1924—is based on the

treatment of 414 cases. The cases were practically unselected, and represent the routine admissions to the hospital during that period. Many of them were very advanced, and, as we review them now, many of them would have been better untreated. The percentage of favorable or operable cases is low, because many cases come to us from other institutions where the earlier cases are kept for surgical care only. No cases are included where there is any question of the diagnosis.

Total Cases	*414*
Known to be dead	181
Lost track of	105

This leaves ..... 128 cases at present under observation, of which 85 were known on April 1st, 1925, to be clinically free from disease. This group of 85 cases is divided by years as follows:

1917	3	
1918	4	
1919	11	
1920	7	
1921	11	
1922	22	
1923	20	
1924	7	(37 other 1924 cases under observation but not yet classed as clinically free)
Total	85	

This gives us a net result in the total group of unselected cases of slightly over 20 per cent. clinically free from disease, which is practically the same as the best surgical figures for the operable group alone. In addition, too much emphasis cannot be placed upon the amount of palliative relief given a very considerable number of the remaining cases, even though their lives were not saved.

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THE TECHNIQUE OF ORAL THERMOMETRY

A. L. MORGAN, '27

Students and practitioners in general are accustomed to regard oral thermometry as one of the few exact procedures of medical practice.

The recognition of slight rises in temperature is of great importance in the diagnosis of early tuberculosis. Palmer, speaking of failures in diagnosis of tuberculous conditions, states, "I am forced to the conclusion that our unfortunate results are due in a large measure to neglect and inaccuracy of simple things, and to no single factor so much as the faulty taking and recording of temperatures. . . . I believe that I am justified in saying that 80% of tuberculous patients, under medical supervision, are treated and discharged without definite knowledge as to whether they are febrile or afebrile."

P. W. Andrus and H. R. Walker of Queen Alexandria Sanitorium carried out a series of experiments to investigate the accuracy of instruments themselves and to determine the time necessary for maximum oral registration.

The results of their experiments were published in the American Journal of Tuberculosis, Vol. IX, No. 3, the main points of which will be considered.

Accuracy of Thermometers

Thermometers of the standard one and two minute variety were used. They were all of the best quality and bore the manufacturer's certificate of guarantee to be correct to 0.2° F. A large waterbath was kept at a constant temperature of 99° F. and the thermometers were tested against a finely graduated thermometer bearing the certificate of the American Bureau of Standards.

The tests determined that:

1. Out of two gross, high grade, new thermometers, seven or about 2.5% were inaccurate by more than 0.2° F.

2. Of 419 thermometers, previously accurate, that had been in daily use for three months, eleven were found to have greater inaccuracies than 0.2° F.

3. Some cheaper thermometers showed errors as high as 2.5° F.

Thus we see that even new guaranteed thermometers cannot be relied upon as accurate, and that they may become defective after use.

Time Element of Oral Thermometry

It is common practice for both the laity and the medical profession to accept, in the specified time, readings from thermometers purporting to register in one and two minutes. On one occasion, an observer in a general hospital noted that the pupil nurse while recording temperatures, removed it after forty-five seconds.

In thirty-two American and Canadian Sanitoria, the prevailing customs in thermometry are as follows:

1. Three record only rectal temperatures.
2. Seven double the time in cold weather.
3. Twenty-nine have chosen the time for mouth reading as follows:

Four use two minute readings
Seven use three minute readings
Fifteen use five minute readings
One uses ten minute readings
Two use fifteen minute readings

The experiments were carried out in order to determine the time necessary for maximum registration, after observing the following precautions.

1. No observations were made within an hour of the last meal.
2. Patients were in bed one-half hour before the temperatures were taken.
3. No drinking or smoking was permitted within one-half hour of the time of registration.
4. Care was taken that the lips were kept tightly closed, and the bulb of the thermometer was kept well under the tongue.
5. Readings were taken without removing the instrument from the patient's mouth.
6. Readings were recorded at the end of each minute and the thermometer retained *in the mouth* until no rise had occurred for five minutes.
7. Patients were on open porches but were not exposed to sun or wind.
8. The outside temperature was warm, the work being done in the summer months.
9. High grade thermometers of the one and two minute variety were used and first tested for accuracy.
10. To establish whether or not the data obtained was peculiar to tuberculous patients, a series of invalids in the wards of a general hospital were similarly tested. The results were in very close agreement.

The data obtained has been summarized in the table

	1 ′′	2 ′′	3 ′′	4 ′′	5 ′′	6 ′′	7 ′′	8 ′′	9 ′′	10 ′′	11 ′′	12 ′′	13 ′′	14 ′′	15 ′′
Time in Minutes	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
Number Reaching their Maximum Reading at Time Indicated	2	5	29	26	26	27	30	26	17	10	9	5	11	2	–2
Percentage of Total Registered at Time Indicated	1	3.5	13	29	29	45	59.5	70.5	79	84	88.5	91	96.5	97.5	98.5, 100

It will be noted that at five minutes only 29% of the total had obtained their maximum elevation and at ten minutes, 84%. The occasional

record showing a rise after fifteen minutes were cases of advanced progressive tuberculosis, and may be presumed to have had an actual increase in temperature during that period.

It will be observed that the maximum number registered in seven minutes. The six to eight minute period represents 42.5% of the total and it falls away rapidly on either side.

The maximum rise beyond the five minute period was 2.2° F., an elevation sufficient to insure the recognition of fever or otherwise. The maximum rise beyond the ten minute period was 0.6° F.

It was observed that in the presence of fever, a longer time was necessary to reach the maximum than in the absence of fever. Of those having a temperature of over 99° F. only 16% reached their maximum in five minutes, as compared to 29% in the entire series. 18% required over ten minutes.

It must be recognized, however, that the average increase in temperature after the five and ten minute periods is rather potential than actual, as far as the presence of fever is concerned. Unless the rise is sufficient to increase the reading to a febrile one, it is of secondary importance.

With this in mind, the figures were studied to ascertain how many came into this group. Of the 200 temperatures recorded, 53 showed readings over 99° F. and were classed as febrile. Of this group of 53, 13 were below 99° F. at five minutes, and the final temperature was over 99° F. So that 24% would have been missed if recorded for only five minutes, and 42% would have been missed if recorded for only three minutes.

Water Bath Readings

The time required for maximum registration of thermometers in a water bath was then studied. Fifty, one and two minute instruments were accurately timed. They averaged fifteen seconds for maximum registration, and were left in the bath for four minutes to ensure that no further rise occurred.

What then is the cause of the discrepancy between oral and water bath time records? The most rational explanation would seem to be that, the mucous membranes of the mouth are normally below body temperature, due to inhaled air. It must require the additional time therefore to allow the temperature of the mucous membranes to approach that of the interior of the body.

To determine if this was true, a small series of patients was examined. The thermometer was placed under the tongue for fifteen minutes. Then it was removed, read, shaken down and replaced, and the time necessary to regain the original reading recorded. The average of the results was one minute. The cause of the difference between these and water bath readings is likely one of contact.

Summary and Conclusions

1. Even certified thermometers cannot be relied upon as accurate, and they may alter with use.

2. The time stated on the thermometer is of no significance.

3. Seventy-one per cent of tested persons failed to record their maximum elevation by mouth in five minutes. Sixteen per cent. failed to record their maximum in ten minutes.

4. Fifteen minutes by mouth is necessary to ensure maximum readings.

5. Forty-two per cent. of patients with fever failed to record fever in three minutes, and twenty-four per cent. failed to register fever in five minutes.

To ensure the detection of fever, put the thermometer well back under the tongue, instruct the patient to keep the lips tightly closed, and leave for at least five minutes, and in particular cases, ten minutes.

ESSENTIAL THROMBOCYTOPENIC PURPURA

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The term purpura is loosely used to designate a group of haemorrhagic diseases, characterized chiefly by haemorrhages, into the skin and from the mucous membranes. As is natural in such a symptomatic classification, the group consists of pathologic conditions due to several different causes, though the result in each case is expressed in a similar fashion. Some recognition of this fact is evidenced by the manner in which we are accustomed to sub-divide the purpuras into sub-groups upon the basis of the clinical picture:—*e.g.*, purpura simplex, purpura symptomatica, Henoch's purpura, peliosis rheumatica and purpura haemorrhagica. Search for a more accurate pathological basis of classification has been difficult and for the most part unproductive. In 1887, however, Denys (1), a French haematologist, made an observation which established a pathologic cause for certain of the purpuras. He noted, in a case of purpura of the type known as purpura haemorrhagica, Werlhoff's disease or morbus maculosa, that the number of platelets in the blood was extremely low. Two years later Hayem (2), also a French haematologist, and himself the discoverer of platelets, confirmed Denys' observation and reported several cases of his own with similar findings. Denys' almost forgotten discovery seems to have aroused little interest until Frank (3) in 1915 reported the result of his investigation, viz., that marked diminution in the number of platelets was a constant feature of that form of purpura known clinically as purpura haemorrhagica.

Numerous investigations since Frank's time have established the fact that many types of purpura, though not all, are accompanied by great diminution in the number of platelets. The deficiency of platelets in these cases is the cause of the haemorrhagic tendency, which appears when the platelets fall below about 80,000 per cubic millimeter, becomes very intense as the numbers of platelets falls still lower, and disappears when the platelets again return to normal. This thrombocytopenia and its accompanying purpura occur in many diverse conditions. Thus, certain intense bacterial infections by staphylococci, streptococci and pneumococci are accompanied by thrombocytopenia and haemorrhagic symptoms. The haemorrhagic form of small pox (Ikeda 4) results

from the intense loss of platelets which occurs in this disease. Certain diseases of the haemopoietic system, (aplastic anaemia, leucaemia and pernicious anaemia,) are sometimes haemorrhagic in form, and when present this is accompanied by thrombocytopenia. Certain poisons, notably benzol, produce an intense anaemia—with thrombocytopenia and haemorrhages. Apart from these cases, however, in which the thrombocytopenia and its accompanying purpura may be regarded as symptomatic of some more serious underlying condition, there exists a group of cases in which the loss of platelets and the purpura are the only evidences of disease. They correspond to the clinical group known as purpura haemorrhagica, Werlhoff's disease or morbus maculosa. On the other hand, there are certain groups of purpura, notably Henoch's purpura and peliosis rheumatica, in which no thrombocytopenia exists.

The thrombocytopenia might be due either to deficient production of platelets or to excessive destruction of them. In the symptomatic group the paucity of platelets does arise as the result of deficient production due to poisoning of the bone marrow in the case of the infections, small pox and benzol; to the crowding out of the megakaryocytes in the leucaemic cases; and to aplasia in the cases of aplastic anaemia.

The explanation of the thrombocytopenia in the essential group is not so simple. Frank believed it to be due to deficient production of platelets as a result of aplasia of the megakaryocytes and classified it as a form of aplastic anaemia. It was not until 1916 that any new light was thrown on the pathogenesis of this condition. In that year Kaznelson (5), a surgeon of Prague, made the observation that in two thirds of the patients the spleen was enlarged. By a happy chance he conceived the idea that this might be evidence of an excessive thrombolytic function on the part of the spleen. He put the question to the test by removing the enlarged spleen from one of his patients, a woman, who for ten years had suffered from purpura with epistaxis and menorrhagia of such severity as sometimes to endanger her life. Splenectomy resulted in a dramatic cure, which seven years later he reports is still maintained. The platelets, which before operation numbered 3000 per cubic millimeter, rose at once following operation to 500,000 per cubic millimeter. As the result of his observation it is now believed that in the essential group of purpuras the thrombocytopenia is due to an excessive destruction of platelets by the spleen chiefly, but to a less extent by the whole reticuloendothelial system. There are many phases of the disease which are not clearly understood, and the mechanism whereby the spleen takes on its excessive thrombolytic activity is entirely unknown, though there is evidence that infection plays an important part in it.

In addition to the thrombocytopenia and enlarged spleen, essential thrombocytopenic purpura displays certain other characteristic features, which it may be of interest to outline. It is a disease which occurs chiefly in female children, unaccompanied by any other evident disease. Frequently it is preceded by an infection of the respiratory tract. Acute forms occur, of abrupt onset and fulminating course, usually fatal in one or two days. They are rare. The chronic form lasts months or

years, may be mild, though usually it is severe, and occasionally is remittant. Haemorrhages into the skin and from the mucous membranes are the outstanding symptoms. In the skin the haemorrhage takes the form of petechiae or ecchymoses. Haemorrhage from the mucous membrane results in epistaxis, bleeding from the gums, haematemesis, and in females, menorrhagia. In 75% of the cases the spleen is sufficiently enlarged to be palpable. The blood changes are striking and characteristic. The platelets are reduced in number. Normally they range from 200,000 to 400,000 per cubic millimeter. In this disease they are never above 100,000, and usually below 50,000 per cubic millimeter. The counts may be as low as 1,000 per cubic millimeter. The haemorrhagic tendency parallels the fall in platelets. The bleeding time is greatly prolonged. The clotting time, however, is normal, though the clot which is formed is soft and defective. It does not retract and extrude serum as does a normal clot. The resistance of the capillary walls is low, so that the slightest injury permits the extravasation of blood. If a tourniquet is placed about the arm at a pressure which will shut off the veins but not the arteries, a numerous crop of petechiae form below the tourniquet in a few minutes (capillary resistance test of Hess).

Interest in this disease has been greatly stimulated by the possibility of its cure by splenectomy. Since Kaznelson reported his first case in 1917, the operation has been performed upon a considerable number of patients. In all, the literature contains reports of about fifty cases. The results have been surprisingly uniform and satisfactory. The operation should be performed only on the chronic form of the disease. In the acute cases the mortality is high and the results uncertain. In sharp contrast to this, when performed upon chronic cases the operation has a mortality of about five per cent., and in practically every case produces a dramatic cure. The platelet count rises at once to a normal level, or even higher. This level is maintained for a week or ten days, and then slowly declines to become stationary at a lower level, normal, or often somewhat below normal. For example, in a recent case, the platelets, which had been 10,000 per cubic millimeter before operation, rose to 65,000 within five hours of the operation, were 144,000 on the following day, and five days after the operation reached the maximum of 1,028,000. From this level they slowly declined, until three months after the operation they numbered 500,000 per cubic millimeter. Coincident with the rise in the platelet count the haemorrhages cease, the bleeding time becomes normal, and the clot retracts. In many cases the ultimate level of the platelet count is subnormal, but it remains sufficiently high to prevent recurrence of the bleeding. It is too early to be certain of the permanency of the results, but there seems every indication that recurrence of the haemorrhagic condition is unlikely.

While the nature of the pathological changes producing the disease are as yet entirely unknown, its symptomatic cure by splenectomy appears to be established upon a firm empiric basis. The cures are as striking as those produced in familial jaundice by the same operation. As our knowledge of haemorrhagic diseases extends, and as the use of platelet counts and the capillary resistance test becomes more widespread, it is

likely that many obscure cases of haemorrhage (persistent epistaxis, menorrhagia of puberty, some cases of haemorrhagic diseases of the newborn) will be found to be bizarre examples of thrombocytopenic purpura and amenable to cure by splenectomy.

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TUBERCULOSIS IN INFANCY AND CHILDHOOD

(*Continued*)

D. S. Bennett, '26 and F. T. Fralick, '26

5. Tuberculous Adenitis

The chief forms of this condition are as follows:

(*a*) *Bronchial*

This condition, although always secondary to some pulmonary lesion, may be the most important lesion present.

The signs and symptoms are very indefinite. The symptoms are usually associated with those of general or pulmonary tuberculosis, and usually follow them. Occasionally, however, the local signs precede all others. They are of a mechanical nature. Pressure upon or irritation of the vagus or recurrent nerves is shown by: cough—hoarse, persistent, and in severe and prolonged paroxysms which often resemble pertussis, but lack the expectoration of the latter; dyspnoea—paroxysmal, often resembling a severe attack of asthma; hoarseness and rarely aphonia. Pressure on the trachea may also show the above signs, but, in addition, the head is thrown back and the dyspnoea is more of an expiratory nature. After some days or weeks sudden death from suffocation may occur. This is due to a large mass of tuberculous debris escaping into the trachea or a large bronchus, through an ulcerated wall. Pressure on the superior vena cava—produces spasmodic dyspnoea, cough, and cyanosis, puffiness and marked oedema of the face.

Physical examination reveals very little. Some men lay great stress on percussion of the mediastinum in the first and second intercostal spaces, close to the sternum, but the results are of doubtful value. To be found in this manner the mass of lymph glands must be very large. Certainly the information gained is of no value, unless taken in connection with a positive tuberculin test and X-ray findings. One sign upon which most emphasis has been laid is that described by *D'Espine*. Many authorities contest the value of this sign. The child must be in the erect position, arms folded, head flexed sharply on the chest, and

whisper, "three," "three," "three." Then auscultate downward over the mid-line of the back, beginning at the sixth or seventh vertebra. Normally the whispered voice ceases at, or just below, the level of the fourth dorsal vertebra. D'Espine's sign consists in the prolongation of the bronchophony below this level. The distinctive quality of the sign is the prolongation of the final "e" for an appreciable time after the voice stops. When this occurs it is suggestive of enlarged bronchial glands.

Eustace-Smith's sign is a blowing venous hum, heard over the sternum just below the notch and also in the jugulars. It is elicited by extending the head as far as possible. It was supposed to be produced in the left innominate vein due to pressure upward by enlarged bronchial glands. Gittings claims this is erroneous and that it is caused by an enlarged thymus gland. The murmur probably originates in the jugulars. Norris and Landis say this sign is of questionable value, since many healthy children show venous hums at the root of the neck.

The most important single factor in diagnosis is probably the X-ray, and next in importance are the signs and symptoms. Enlarged bronchial glands are usually tuberculous. Hodgkins and malignant disease are rare in children. Laryngeal diphtheria may be hard to rule out when few signs of tuberculosis are present.

As long as the disease remains confined to the lymph nodes the child is not usually in danger. Spontaneous cure may result by encapsulation or calcification.

Treatment

Treatment is constitutional if no signs are present. If the latter condition occurs the child should be taken to a hospital, where he is under observation and may be examined with a bronchoscope.

(*b*) *Cervical*

This condition is not as common in this country as in England.

In the early stages all that is found is a gradual, slow, bilateral enlargement of the glands, appearing as a rule in front of the sternomastoid muscle. Later the condition becomes unilateral.

In the acute form there is an acute swelling of the glands with redness, tenderness and fever, reaching a maximum in 3-4 days and then persisting.

The chronic has an insidious course, extending over months or years, with repeated exacerbations. About one-half the cases go on to suppuration. Others may disappear spontaneously. As the condition progresses the glands become matted together, and fixed first to the deeper structures, then the skin and finally soften and discharge the typical tuberculous pus.

Characteristic of this condition is the presence of a swelling, occurring as a rule along the anterior border of the sternomastoid muscle, with an insidious onset and slow course. It is most frequent between the ages of two and ten years, and is accompanied by a positive tuberculin test. Malignant growths, Hodgkin's diesase, and syphilis are rare in children.

Cervical tuberculous disease seldom is the direct cause of death. Ultimately the cases recover but there is often a very protracted course.

Treatment includes: (i) removal of tonsils and adenoids if at all diseased; (ii) constitutional treatment; (iii) operative measures, which are indicated when there has been no improvement for 3-4 months under the above treatment, and the glands increase in size and number or begin to soften. Thorough removal often cures.

(*c*) *Mesenteric*

Apart from slight toxic effects of tuberculous infection it is doubtful whether symptoms are produced by disease of the glands themselves unless they attain a large size, or suppurate and involve other structures.

Repeated attempts at palpation of the abdomen, when the muscles are relaxed and intestines not distended, may disclose large glands, usually by pressure against the vertebral column on the right or left lower quadrant of the abdomen. Rarely they can be felt through the rectum and thus are differentiated from other enlargements.

Diagnosis of simple mesenteric enlargement is theoretically possible but very difficult.

The prognosis is at least as favourable, if not more so than that of tuberculous disease of the bronchial glands.

Treatment is constitutional unless complications arise.

6. Tuberculous Enteritis

Intestinal tuberculosis is most common between the ages of three and eight years. The disease as found in infants and young children, is usually mild in character.

Signs and symptoms are exceedingly untrustworthy.

Diarrhoea, or a tendency to this, is the most frequent symptom of ulceration and may be very obstinate. There is colicky pain in the abdomen, worse before stool, but present at irregular intervals. Blood or pus in the stools is not very frequent. Fever is only very slight. Examination of the abdomen shows nothing characteristic. There may be moderate tenderness, especially around and below the umbilicus. Positive diagnosis can be made only at operation or autopsy. The disease differs from dysentery in having a more gradual onset and less severe course. A large haemorrhage from the bowel is in favour of tuberculosis. Most suggestive is a patient who has a tuberculous lesion in the lungs, showing diarrhoea.

It is extremely rare for the intestinal lesion alone to be the cause of death. For infants the best diet consists of protein milk or L.A.M., with the addition of dextri-maltose. For older children fresh fruit juice without the pulp, strained vegetable broth or meat broth, soft boiled eggs, custard and junket may be given in suitable cases.

7. Tuberculous Peritonitis

This occurs most frequently between the ages of one and five years.

The essential symptoms are emaciation, colicky pains, irregularity of the bowels and usually slight but continuous fever. The abdomen is enlarged, often with evidence of fluid. Nodular masses may be felt on careful examination. The umbilicus may be pouting, with a definite induration about it. In young children chronic ascites usually means tuberculous peritonitis. Abdominal paracentesis to obtain fluid for diagnosis is dangerous and not justifiable.

Under two years the condition is fatal, but after this age the outlook is hopeful, more especially if fluid is present. In older children many cases recover spontaneously. It is usually advisable to operate in the case of the ascitic form which has not improved after a fair trial of constitutional treatment. Also in either form, if abscess formation, obstruction, or other complications develop, operation may be necessary.

8. Tuberculosis of Bones and Joints

This phase of the subject belongs more especially to the domain of orthopedic surgery, and will only be mentioned here. The important points to note are pain, muscle-spasm, limitation of movement, atrophy, deformity and X-ray findings.

Prognosis

Many writers state that there is practically no such thing as a healed or latent tuberculous infection in children under two years of age, but that the condition is always active and the outlook almost hopeless. By the tuberculin skin reactions it has, however, been shown that tuberculosis in children is not so invariably fatal. Dr. Davis, from a survey of the records of the chest clinic and wards of the H.S.C., Toronto, studied the death rate in such children. Of 2,300 cases he found that 68 gave a positive tuberculin test. At least six months after the test it was found that of those under one year 70% died, and of those between one and two years of age 24% died, while in the two groups the combined death rate was 44%. Dr. Alan Brown found that the mortality was somewhat higher than this. He showed in a certain series that 70% of hospital cases under two years giving a positive reaction to the tuberculin test proved fatal. The positive test is usually due to a chronic infection from which the death rate is negligible. The acute form develops within two months of infection. Thus, if an infant who gives a positive test is protected from possible reinfection and remains well for two months, he is likely to recover. Death always results from broncho-pneumonic, miliary, or meningeal tuberculosis. In older children the acute forms are less common. Death may sometimes occur from one of the chronic forms.

Prophylaxis

The first responsibility lies with the obstetrician. He should be able to detect, before birth of the child, tuberculosis in the mother, and prepare for the decision of absolute separation of the offspring from the tuberculous parent. Either the mother or the child must leave home. Probably the best solution is the removal of the mother to a sanatorium as soon as she is fit, there being rigid interdiction of any close contact with the child up to that time. In other cases the child may be taken within a few days after birth to a preventorium, or another home. Such precautions should be carried out even if the diagnosis is not certain. Before the baby's birth the house should be thoroughly cleaned and exposed to fresh air and sunshine. Raising of a dust in the house should be avoided. There should be thorough washing of toilet articles, etc., and scalding of the baby's eating utensils. In selecting a nurse for the child one must be sure that she is not tuberculous. In a similar manner

older children should be protected from the disease. Other members of the household must be investigated for possible tuberculosis, and if such are found they should be isolated.

Constitutional Treatment

1. The Potentially Tuberculous Child

(*a*) *Environment.*—The child should be kept in a clean, dry environment with plenty of sunshine and pure air. To obtain fresh air in the winter the child is dressed in his out-of-door clothes while the windows are opened. He should sleep in a room preferably with two open windows. A sleeping-bag and cap should be worn. The baby should be kept off the floor by means of a baby pen. In older children a special play room is useful; the playground is very advantageous. Open air schools are of great value to the general health. The child should have frequent outings to the country.

(*b*) *Diet.*—The nutrition of the child must be maintained. If possible a healthy wet-nurse should be obtained. Otherwise simple dilutions of whole cow's milk as for a normal infant are best. In older children as much fat as can be digested should be given in the form of fat meat or cream. A steady gain at or near the average weight is desirable. There should be frequent examinations, preferably every three months, best in the afternoon. The temperature and weight should be known. A careful physical and X-ray examination, from time to time, if the results are compared, may be useful.

2. The Clinically Tuberculous Child

To successfully treat a tuberculous child one must impress upon the parents the necessity for complete compliance with orders.

(*a*) *Environment.*—For children over ten years of age usually permission can be obtained for treatment at a sanatorium, by which permanent cure is most likely to result. Otherwise treatment should be carried out somewhere near the patient's home where the air is pure and sunshine is abundant. Heliotherapy is especially of value in tuberculosis of bones and joints, cervical nodes, peritoneum or skin. Rollier's method consists of first exposing the feet to the direct rays of the sun for five minutes three times daily. This is gradually increased to reach a maximum of exposure of the entire body for from 5-7 hours a day. In the early stages, with constant fever, there should be absolute rest in bed, continued as long as the temperature and pulse are elevated, and while toxic symptoms persist and the lesion shows any signs of progression. Two weeks after the temperature and pulse have subsided exercise should be begun gradually. This may be allowed for ten minutes at first and increased by 5-10 minutes per day, if no symptoms result. When a child can engage in exercises for 4-5 hours per day without symptoms, for three months, the condition may be considered as arrested. The child should be out-doors during the day, and at night is best in a sleeping porch, in order to get all the fresh air possible. Ample and suitable clothing should be worn. In bed cases there should be extra covering over the feet and legs. A knitted cap or helmet is essential.

(*b*) *Diet.*—During absolute rest care must be taken to avoid digestive disturbance. In the first year milk is the essential food. During the second year not more than three pints per day should be given. One fresh egg a day is beneficial. After the second year foods to stimulate the appetite should be given. These should include ice cream and simple home-made deserts, with due care to avoid excess carbohydrate. A diet containing abundance of fat is helpful. A higher caloric diet than is normal for the child may be given if it can be digested.

(*c*) *Specific Treatment.*—Most authorities consider tuberculin treatment in children to be of some value in all but the pulmonary type. Gittings believes that it does good merely by increasing the blood supply and subsequent scarring of the diseased focus. Each case should be considered carefully before such treatment is begun. It is contra-indicated in nephritis, decompensated heart disease, acute infections of any kind, diabetes mellitus, where fever is present, and when the tuberculous lesion is very advanced. Dilutions of O.T. tuberculin are used subcutaneously. It is necessary to begin with a very small dose and to increase this gradually. For the average child of 2-3 years the proper initial dosage is .00002 mgm. If there is any fever following the injection the dose should be diminished to one quarter the amount and then gradually increased. Injections are repeated every 4-5 days, doubling the dose each time as long as no systemic reaction occurs, until the dosage reaches .05 mgm., when it should be very cautiously increased, and never more than .1 mgm. After several months, treatment may be stopped for an interval of a few months.

(*d*) *Symptomatic Treatment.*—This is of great importance, as every symptom tends to wear out the patient.

Fever rarely demands treatment. In hyperpyrexia, sponging or bathing may be useful. Anorexia—Give plenty of fresh air and a complete change of diet. Stop all sweets and decrease the amount of milk. Biliousness—Carefully try exercise. Completely withdraw solid food and milk and give clear salt soup and plenty of water. Cough—If productive, should not be stopped. If the cough is not useful, and is exhausting, small doses of codeine sulphate is the best sedative. Anaemia—Give a liberal diet containing green vegetables. In infants egg yolk, scraped beef, prune pulp, or spinach may be given. Asthenia—Fresh air, good food and rest are essential. Insomnia—Avoid excitement in the afternoon and give a hot drink of milk at bed time.

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SITUS VISCERUM INVERSUS

A. R. Armstrong, '29.

Situs viscerum inversus or heterotaxy may be defined as that congenital anomaly in which the relation of the parts is so altered that the organs which ought to be on the right side are found on the left, and conversely. There is an inversion of parts such that if the thoracic and abdominal cavities be laid open their contents appear as seen in a mirror. Hence the phenomenon is often spoken of as mirror-imaging. Though comparatively rare, the condition has been known for a long time. Aristotle (1) clearly observed it in quadrupeds, but there followed a long period of silence on the subject until the 17th and 18th centuries, when physical diagnosis by percussion and auscultation became more perfected.

The anatomical relations obtaining in heterotaxy are, in general, as follows (2): In the thorax the oesphagus passes from the middle line towards the right half of the diaphragm. The right lung has two lobes and the left three, and the bronchi also are inverted. The axis of the heart and pericardial sac is directed obliquely downwards and to the right; and about two-thirds of the organ lies to the right of the middle line and only one-third to the left. The cardiac apex lies in the right mamillary line, corresponding to the fifth rib or intercostal space. The pulmonary veins open into the right auricle, and the corresponding ventricle gives origin to the aorta; the left auricle receives blood from the superior and inferior cavae and from the coronary veins, while the left ventricle sends it on to the lungs in the pulmonary artery. A two-segmented valve divides the two chambers of the right heart, while a three-segmented one divides the left heart. The pulmonary artery arises from the left ventricle and passes obliquely to the right; it divides into two branches in the concavity of the aorta, the shorter of which goes to the right lung and is connected with the ductus arteriosus. The same inversion affects the aorta both in its arch and in its descending part, the great vessels which arise from it, the great veins, the thoracic duct, the phrenic, pneumogastric, and sympathetic nerves, and the smaller vessels of the thorax. The diaphragm also exhibits similar changes, those openings in it which are normally on the left side being found on the right, and vice versa; and its level on the left side is higher than on the right.

In the abdomen, the stomach is found on the right side, where its greater part occupies the epigastrium; and the whole organ has a direction from above downwards, from before backwards, and from right to left. The duodenum has its concavity facing the right; it is directed upwards to the left and backwards, and then turns vertically downwards and proceeds from left to right to become continuous with the jejunum. The large intestine from the caecum to the sigmoid flexure is exactly transposed. The pancreas has its head to the left and its tail to the right side, and lies in the cavity formed by the inverted duodenum. The spleen is on the right side, while the larger lobe of the liver is on the

left, and the smaller lobe comes into relation with the stomach on the right side. The gall bladder and ducts are on the left side. The right kidney is at a higher level than the left. The abdominal aorta, the portal vein, and the vena cava inferior, as well as the other vessels, are all exactly inverted.

The existence of atypical cases is much doubted. Most investigators are inclined to believe that in true heterotaxy all organs are similarly affected. The cause of the doubt seems to be the inability to distinguish between situs inversus and transposition of certain organs due to a pathological mechanism. There is, however, no reason to believe that the anomoly is in any way pathological, nor that any transference of parts occurs.

Heterotaxic subjects are usually unaware of their condition, and it is only detected in many cases by accident, as, for example, in an examination for life-insurance, military service, etc.; but from the above description of situs inversus it can readily be seen that, although it is not common, it is important in its clinical aspects; and while it may have no prejudicial effect on the life and health of the individual, it is liable to prove a difficult complication in surgical procedures. Changes in the methods for the performance of most operations, such as oesophagotomy, paracentesis thoracis, and those on the stomach, spleen, liver and gall-bladder, etc., would be essential.

The diagnosis, while it presents some difficulties, is usually accomplished with ease. At birth it may well be suspected if the cardiac impulse is seen to be on the right side. But this sign is common to heterotaxy and the anomoly of diaphragmatic hernia, so that a more thorough investigation must be conducted. Great accuracy in diagnosis may be had by means of percussion, auscultation, mensuration, and skiagraphy. In men the fact that the right testicle hangs lower than the left may be taken as an outward sign. Left-handedness is not well correlated with the condition, although it is noted rather more frequently than in individuals with situs solitus. This functional peculiarity is usually forcefully repressed by convention from childhood on, and it is of interest that some individuals with situs inversus, when instructed to write with the left hand, make mirror-image writing.

The development of situs inversus is not yet fully understood, and many theories have been brought forward. Extensive observations on twinning have been carried out by H. H. Newman with the armadillo (3). This animal regularly gives birth to quadruplets, from a single fertilised egg. Although situs viscerum inversus rarely occurs, mirror-imagining of structure derived from the ectoderm is very common, and it was believed that quadruplets were formed by a fission process. Newman considered that symmetry among quadruplets was the result of an intricate interplay of grades of successively operating systems, the latter tending to obliterate the effect of the former, but not always successfully. In general, mirror-imaging is evidence of a residuum of a bilateral symmetry that held sway in the blastocyst before fission began. When the primary outgrowths are formed they are the products of antimeric halves of the first embryo, and should therefore show mirror-

image relations. But a partial physiological isolation of the two halves permits a certain reorganisation, which tends more or less to destroy most of the original symmetry. In the armadillo no visceral transposition takes place, since twinning is initiated and carried out in the ectoderm, involving the entoderm only passively. It is remarkable that the same situations of symmetry reversal occur in both armadillo and human monozygotic twins, and Newman believes the phenomenon the same in both cases. If this is so, since it is the uncommon thing to twin the human, it may be that the mechanism is not so efficient, and might in some cases involve the entoderm in the process. Hence it would be of great interest to obtain figures of individuals with situs inversus who display mirror-imaging of ectodermal structures, although the reverse correlation is known to be zero.

That monozygotic twinning could be the cause of situs inversus has been strenuously disputed, because it is only occasionally that one of monozygotic twins has the anomoly. But as it was pointed out above, the entoderm becomes involved only passively, and the ectodermal structures, such as the friction ridges on the palms of the hands and soles of the feet, are very often reversed. So far in no case of situs inversus has a duplicate twin been observed. But this would not be remarkable if we considered the involvement of the entoderm as the result of a pathological condition such that the death of one foetus would result. If the foetus whose organs would thus become reversed was the survivor, an individual with inversed viscera would be born along with a twin embryo with situs solitus whose death occurred at such an early stage of development that no recognisable trace of it would be left. The chief difficulty in reaching a definite conclusion is that too few cases of heterotaxy have been studied on which to base a conclusion.

A theory of situs inversus, which at first seemed plausible, was the idea that, at least in the chick, the lateral displacement was effected by the position in which the embryo lay in the early stages of development. The chick embryo normally lies on its left side. It was found that inversion could sometimes be effected by reversing this position. But the theory was broken down by the fact that some embryos found to be lying on the opposite side to normal did not show situs inversus.

Dareste believed that the anomoly was dependant upon the unequal length of the paired tubes which form the embyonic heart. In order to put this to a test he caused the left cardiac tube to grow faster than the right, which is normally larger, by unequal heating of the right and left vascular areas. In this manner he was sometimes able to produce heterotaxy. But Dareste's theory starts at too late a period of development. It fails to explain why one tube grows faster than the other under normal conditions. When applied to the theory of twins, however, it becomes more useful. If, as in the case of monozygotic twins, the embryos were close together, in some cases they might be so close that the field of blood supply on the left of one would interfere with that on the right side of the other. If this occurred it might be expected that one embryo would have the right cardiac tube longer than the left,

and that the reverse condition would obtain in the other embryo. Hence inversion would occur in the left hand embryo and situs solitus in the right. But in our present state of knowledge, any theory depending for strength on the twinning theory is thereby weakened.

There is an inclination to carry the time of production of situs inversus back to the germinal period. This is supported by the morbid assymmetry displayed in certain invertebrates. It consists in a twisting of the whole body of the animal. Occasionally a complete reversal of the twisting occurs in some gastropods of the mollusca (4). And in such cases the change must take place at a very early period. That the initial structure of the germ need not be unnecessarily complicated by imagining it to comprise an enormously large number of so called determinants, but that, given a certain number to start with, the rest will follow by the actions and interactions of these upon one another, was shown by Spemann and Pressler (5). A square piece was cut out of the back of an amphibian embryo, in the medullary fold stage, turned right around so that its anterior end faced posteriorly and its right side the left, and then grafted in again. The part removed involved the nervous system, notochord, some mesoderm, and the roof of the gut. The embryo continued to develop and showed inverted viscera, and inverted heart.

Concerning what has been said, it is doubtful how far it is wise to make deductions on experiments with the lower animals. It is seldom that a chance of studying situs inversus in utero occurs in the human being. Surgeons should therefore be exhorted to take advantage of any opportunities afforded them. So far two things are known definitely, viz.: true heterotaxy does not occur after the organ has once commenced lateral displacement, and it is not transmitted by heredity. Finally it might be suggested that the difficulty of determining the causation factor may in part be that heterotaxy may be brought about by more than one series of conditions, as seems probable in considering the result of Pressler's experiment and that of Dareste's.

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THE CAPILLARY CIRCULATION AND ITS RELATION TO SURGICAL SHOCK

B. R. Dickson, B.Sc. (Med.), '26.

With the increased activity of a given organ or tissue, there is associated a greater oxygen requirement, this usually entailing a larger supply of blood. Whether this demand for oxygen or blood is general or local, the adjustments of the peripheral parts of the circulatory

system plays a very important role in achieving a proper regulation of the circulation and ensuring that the demands from all parts are met with as adequately as the existing conditions will permit.

It is the capillary system which accomplishes the ultimate purpose of the circulatory system, enabling the blood to discharge its proper functions of supplying material to and removing waste from the tissues. The total capillary blood-flow is dependent upon the ever changing calibre of the arterioles and venules supplying the part.

Until recently, the capillaries were viewed merely as minute but purely passive conduits for blood; but it is now conclusively proven that the capillaries are capable of active and independent contraction according to the demands of the tissue which they supply. The first clear demonstration of active capillary contraction seems to have been given in 1879 by Roy and J. Graham Brown. The monumental work of Krogh shows that in contracting muscles, not only are more capillaries open, but also that the average diameter of the capillaries which are open is greater than in the resting muscle.

Hitherto, the capillaries have generally been thought of as mere tubes of endothelium. Recent microscopical evidence contributed by Vimtrup demonstrates that the contractile structures associated with change in capillary calibre are branched cells placed outside the walls of the capillaries, these cells being very transparent, and demonstrable only with some difficulty. These may be called Rouget cells, after Rouget, who originally described them in 1873, and are a special variety of smooth muscle cell placed at intervals along the capillaries. As a clinical guide, one may assume that the colour of the skin is determined by the number and degree of filling of, and rate of circulation in, its capillaries, while the surface temperature depends upon the rate of circulation through its arterioles.

Experimental physiology has demonstrated that certain substances, when injected into the blood stream, cause an extreme dilatation of the capillaries, and to these the name of capillary poisons has been given by Heubner. The investigations of Dale and his collaborators in which histamine was employed form the most useful study in this field. Evidence obtained by the use of plethysmographic and perfusion experiments shows that histamine brings about a dilatation of the capillaries and a constriction of the arterioles. Dale and Richards further demonstrated that, after recent section and even after degeneration of all the nerves to a limb, the dilator effect of histamine was not abolished, but in most cases much intensified.

The Reactions of Capillaries to Stimuli:

The capillaries have a vasodilator supply very similar to that of the arterioles, stimulation of the posterior nerve roots causing dilatation of both capillaries and arterioles. Thus, in herpes zoster, a condition in which there are local areas of skin flushing associated with irritative lesions of the posterior nerve roots, the dilatation affects both types of vessels. Further, it has been demonstrated that the hyperaemia resulting at the site of application of mustard oil depends on the integrity of the

nerve supply, and that it disappears after the induction of local anaesthesia by novocaine. Non-medullated fibres are found in close relation to the blood capillaries, and are considered to be of sympathetic origin, forming a terminal nerve net of primitive type about both capillaries and arterioles. On stimulation of these fibres, contraction of both types of vessels has been observed. The application of warmth brings about relaxation, and cold produces contraction, of the capillaries, these effects being due partly to local stimulation and partly to an effect on the nerves.

Capillary Pressure:

The pressure in the capillary circulation is low, but varies considerably, being raised by a dilatation of the arterioles and lowered by arteriole constriction. Capillary pressures in the human hand have been measured by Carrier and Rehberg, who ascertained that it varied with the position of the hand with reference to the heart, ranging from a pressure of 30 cm. water to one of 4 or 5 cm. In the feet the capillary pressure is normally maintained at a low level by the presence of valves in even the smallest veins, and by the occurrence of constant small muscular movements which force the blood into these veins.

Capillary Permeability:

The thin capillary walls allow a ready diffusion through them of water and crystalloid substances, but hold back more or less completely the proteins and other colloids of the blood. The fact of prime importance in connection with capillary permeability is that it is increased under any circumstances which bring about a dilatation of the capillary vessels. It was observed by Dale and Laidlaw that histamine administration resulted in a rapid concentration of the blood cells, this being attributed to an increased rate of capillary filtration. These workers further showed that with histamine there is a considerable increase in lymph flow from the thoracic duct, and also a diminution of the blood volume. The production of oedema occurs when there is a decreased resistance to filtration through the capillaries in any region, or when the capillary pressure is abnormally high, the latter being present in certain heart affections and in pregnancy.

The Action of Chemical Substances on the Capillaries:

The studies of Dale and Richards also provide evidence that the presence of adrenaline in the blood stream can improve the tone of the capillaries. Carbon dioxide and other acids bring about a relaxation of the capillaries, and oxygen deficiency has the same effect. In the opinion of Dale, adrenaline is probably the chemical factor which is chiefly responsible for the maintenance of capillary tonus. Krogh, on the other hand, believes that a pituitary hormone is the chemical factor chiefly concerned, but there is no conclusive evidence in favour of either of these substances. In the laboratory of Sir Thomas Lewis it was shown that one of the active principles of the pituitary body exerts a considerable action on the capillaries, producing extreme pallor of the skin without any marked increase in blood pressure. Also, according

to Krogh, the injection of pituitary extract will restore blood pressure after the profound vascular shock induced by the administration of histamine. However, Dale has demonstrated that after the removal of the suprarenals from a cat the cat becomes exceedingly sensitive to the action of histamine, and Kellaway and Cowell have obtained further evidence suggesting that adrenaline and histamine are physiological antagonists.

The Secretion of Urine:

Modern views of the capillary circulation introduce an entirely new factor into the problem of urinary secretion. Until recently, it has been tacitly assumed that all the glomeruli were constantly open to the circulation. Richards and Schmidt have contributed evidence that the kidney glomeruli have periods of constricted closure which alternate with periods during which they allow blood to flow through them.

Surgical Shock:

The possible variation in capacity of the capillary system is enormous. The alterations in the vascular capacity that may result from a wholesale opening or shutting down of the capillary beds are far greater than could be effected by any ordinary changes in the tonus of the arterioles. According to Krogh, the volume of blood in the active muscles of a guinea-pig may be 275 times as great as when at rest, and even this represents only a third of the possible volume if all the capillaries were fully dilated. Hence, whenever an extensive dilatation of the capillary system occurs, we must consider not only the reduced peripheral resistance, but also the tremendously increased capacity of the vascular system. Following the administration of histaminė, and the consequent capillary dilatation, there is a seeming disappearance of blood from the circulation, and the animal "bleeds into its own dilated capillaries", the heart and veins becoming emptied, so that the heart, though beating as vigorously as ever, has an extremely small output. Besides this, as already mentioned, there occurs an actual loss of fluid by percolation through the walls of the dilated capillaries, resulting in a real loss of fluid from the circulation as well as the apparent loss described immediately above.

These facts are vitally related to the pathology of surgical shock, or "secondary shock", and the shock-like state of collapse which is often observed in the terminal stages of general infections. Surgical shock is essentially a condition of diminished blood volume. This loss of blood volume is often partly due to haemorrhage, but results chiefly from (a) loss of plasma by filtration to tissues, (b) stagnation of blood in the peripheral parts of the circulation, especially the capillaries. Similar factors are at work in the generalised infections.

The excellent investigations in this field, as carried on by Dale and Laidlaw, emphasize the close similarity between these conditions and the shock induced by massive histamine administration, and would strongly suggest that the clinical conditions are due to the action of histamine or substances exerting a similar action, and which are produced

as the result of tissue damage. It is possible to extract histamine from nearly all tissues after death, and substances resembling histamine, and it forms an attractive hypothesis to suppose that such substances, liberated from tissues damaged in the course of accidents or operations involving much handling of tissue, may find their way into the general circulation, thus establishing the familiar picture of shock. Experimental proof of this has been provided by Cannon and Bayliss and others, who have shown that the crushing of a limb in an anaesthetised animal results in a shock-like state; but if the vessels of the injured limb are occluded previous to the mechanical injury, shock does not appear until the vessels are released, allowing the products of trauma to pass into the general circulation. In this connection, it is interesting to note that exposure to cold, haemorrhage, or anaesthetics, such as ether or chloroform, lower the resistance of the animal both to the action of histamine and to the intervention of surgical shock. Dale maintains that nitrous oxide does not exert such an action, and does not tend towards the production of this condition.

Mild Tissue Trauma and Capillary Dilatation:

Recent studies by Sir Thomas Lewis and his co-workers suggest that the production of histamine or histamine-like substances in proportionately smaller amount may result from even mild injury to tissues, and may account for the transient dilatation of skin capillaries which is brought about by such very limited damage as is done in demonstrating the red tache, and the raising of wheals. Lewis and Grant were able to produce similar wheals by the inoculation of histamine into the skin. Further, this hypothesis may apply to the causation of skin reactions, oedema, wheals and blisters, by such other injuries as are produced by scratches, pin-pricks or the application of heat.

Thus, we may consider the production of histamine by the tissues as a physiological process prone to be set in motion by the limited trauma encountered in ordinary daily life. Adrenaline may be regarded as the normal antagonist to this action, preventing its consequences from reaching undue proportions. In view of this supposition, one should reconsider the abandoned hypothesis suggesting that supraranal exhaustion is concerned with the onset of surgical shock, whereby the normal resistance of the body to large amounts of capillary poisons is removed.

THE PATHOLOGICAL FINDINGS IN POLIOMYELITIS AND POLIOENCEPHALITIS*

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The pathological findings in this disease may well be considered under three headings, viz.:

*This and the following article complete a series of three papers on the subject of Poliomyelitis delivered before the Academy of Medicine, November 26th, 1925. The first of the series appeared in the Medical Journal, February, 1926.

First. The etiological factor in the production of the disease.

Second. The changes that take place in the human body which can be demonstrated by clinical laboratory tests, and

Third. The changes in the body as demonstrated by post mortem examination.

I. Etiology.

Three views in particular have been advanced.

(1) That of Saunders, which we shall designate the "fly theory". Saunders claimed that the virus has a habit outside the human body; that it is developed to full potency in the green fly and its larvae, and that it may be transmitted by the ingestion of these larvae, or by the bite of the green fly. This view appears to have received comparatively little support.

(2) The second view is that of Rosenow, who claims that the disease is due to a pleomorphic, green-producing, aerobic streptococcus, which possesses strong antigenic properties, and can, therefore, be used for the production of a thereapeutic anti-serum by inoculation of horses.

I have been unable to find any confirmation of Rosenow's work.

(3) The third view, and the one which appears to be quite generally accepted at the present time, is that the disease is due to a filterable virus, which can be obtained from the washings of the nasopharynx and from intestinal excreta of infected animals. Flexner and his co-workers have succeeded in infecting monkeys by intracerebral, intravenous and intra-peritoneal inoculations.

II. We shall now consider the changes which take place in the body which can be demonstrated by post-mortem examination.

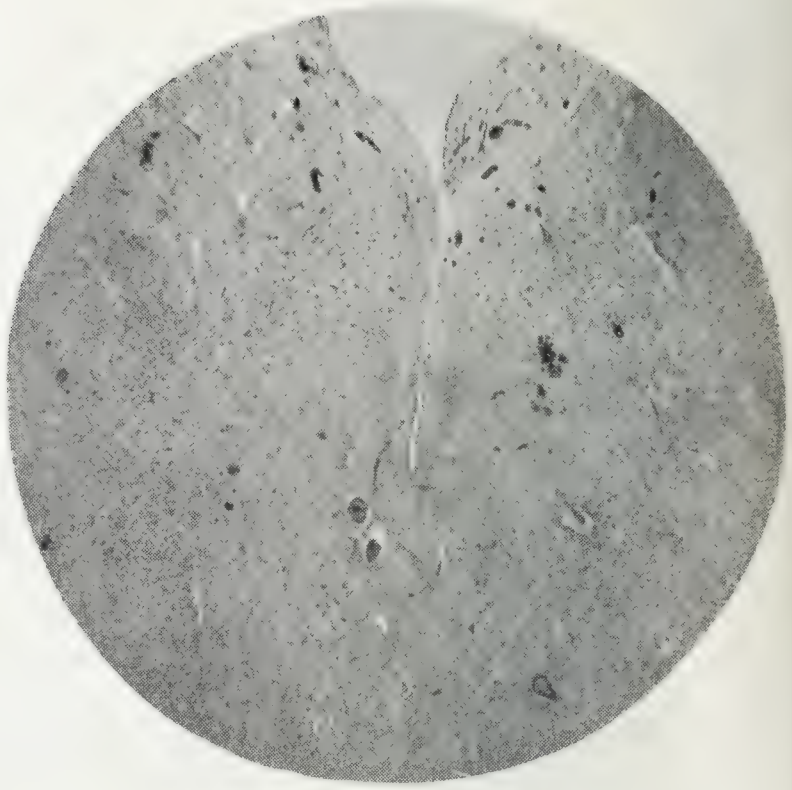
The term anterior poliomyelitis would seem to suggest that the inflammatory lesions of this disease are confined to the anterior horns of the gray matter of the spinal cord. This, however, is not the case. Not only do changes occur in both anterior and posterior horns, but also in the white matter of the cord and medulla, in the meninges and various other organs of the body. This would seem to indicate that the disease is the result of a general rather than a local infection.

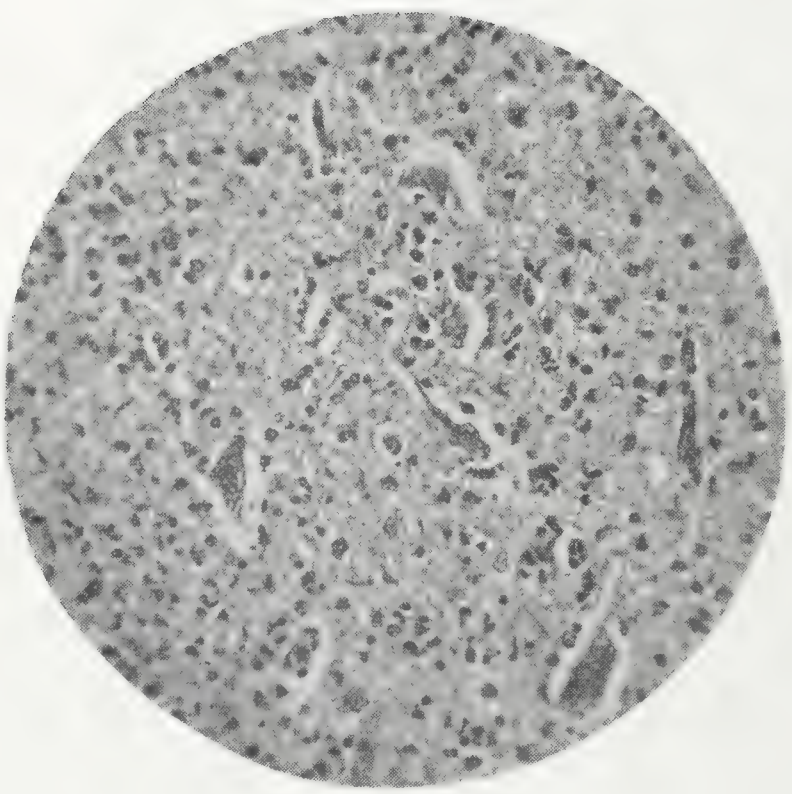
The lesions outside the central nervous system include chiefly changes in the liver and lymph glands. In the liver we have seen cloudy swelling, fatty degeneration, focal necrosis, with polymorphic and lymphocytic infiltration in and around the areas of necrosis, and periportal lymphocytic infiltration. The changes in the lymph glands consist chiefly oedema, congestion and infiltration with large, phagocytic mononuclear cells, such as are seen in typhoid fever.

The changes in the central nervous system are the most characteristic and constant. In the gross one may see very little other than a diffuse congestion of the meningeal vessels giving the surface of the cord and brain a dusky hue. At other times the larger vessels stand out quite prominently. Cross section of the cord at various levels may reveal a reddish tint in the cut surface due to congestion and haemorrhage. This is usually most noticeable in the gray matter, but this is probably due to the fact that this portion of the cord is more vascular.

Fig. 1

Fig. 2





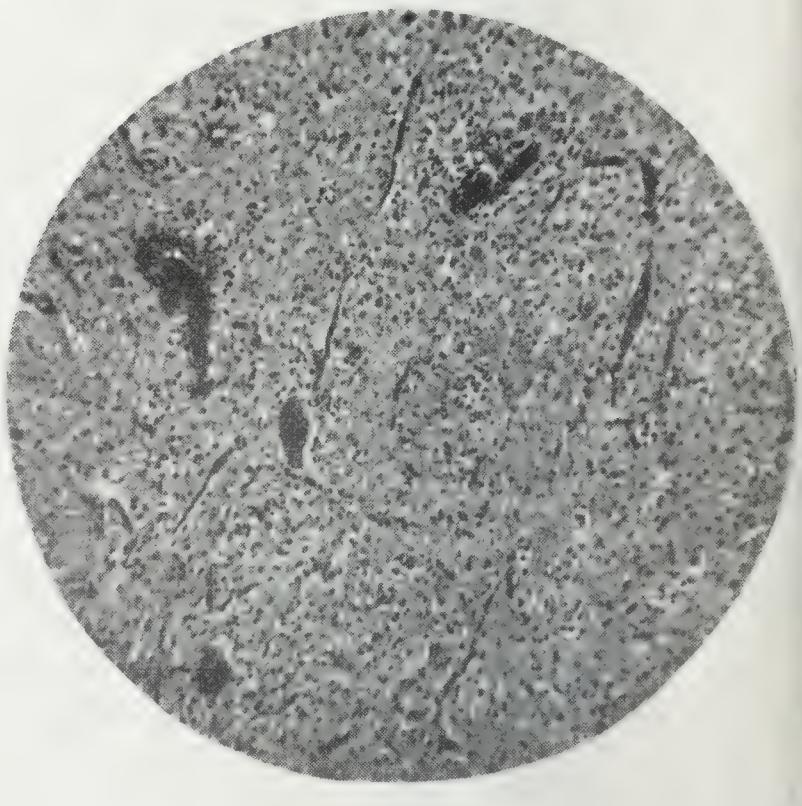


Fig. 4

Fig. 3

Fig. 5

Microscopically the various changes can perhaps be best illustrated by the accompanying microphotographs:—

FIG. 1. This is a section of medulla from a boy 12 years of age who died in the Hospital for Sick Children, 6 days after the onset of his illness, with intercostal and diaphragmatic paralysis. This shows congestion of the meningeal vessels, some cellular exudate in the meninges, and congestion of the vessels of the medulla with perivascular lymphocytic infiltration. (x 16.)

FIG. 2. From the floor of the 4th ventricle of the same case, higher magnification. This shows oedema, congestion, haemorrhage and perivascular infiltration. The nerve cells here are still intact. (x 25.)

FIG. 3. Same case, just below the floor of the 4th ventricle, showing congestion, perivascular infiltration, slight diffuse infiltration and well preserved nerve cells. (x 94.)

FIG. 4. Same case. Cervical enlargement of the cord showing diffuse infiltration with both polymorphonuclear leucocytes and lymphocytes, also badly damaged anterior horn cells. (x 375.)

FIG. 5. From a girl 27 months old who died on the 7th day of the disease. This is a section through the cervical enlargement (anterior horn region). This shows congestion, haemorrhage, diffuse infiltration and a very few small degenerated nerve cells. The majority of these cells have disappeared entirely. (x 94.)

SIGNIFICANCE OF FIGS. 3, 4, and 5.

FIG. 3. Shows well preserved nerve cells in an inflammatory area. Clinically the corresponding muscles would probably show some weakness and twitchings, but no definite paralyses.

FIG. 4. Shows badly damaged, but still living, nerve cells. Here the corresponding muscles would, no doubt, show paralyses which, after a time, would disappear and the muscles recover.

FIG. 5. Shows an area in the anterior horn in which the great majority of the nerve cells have disappeared. Here, had the patient recovered, the paralyses would, no doubt, have been permanent.

SUMMARY.

To sum up we would say:—

(1) That the causative factor in this disease appears to be a filterable virus.

(2) The principal changes demonstrable by clinical laboratory tests are those in the cerebro spinal fluid.

(3) The post mortem findings include toxic lesions in various viscera with the most marked changes in the spinal cord and medulla.

Of the changes that take place in the human body, which can be demonstrated by clinical laboratory tests, those in the cerebro spinal fluid are the most important. The blood changes are inconstant, and do not aid materially in the diagnosis of the disease. Inasmuch, however, as the spinal fluid changes are so intimately associated with the diagnosis and prognosis, we shall leave this phase of the subject to be discussed by Dr. Hart in his paper on the clinical aspects of the disease.

CLINICAL ASPECTS OF POLIOMYELITIS

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Poliomyelitis is one of the diseases the diagnosis of which is very frequently missed in the early stages, so that if one can recall some of its clinical characteristics it may be beneficial.

Drayton has described poliomyelitis under three distinct groups.

First Group—Shows two distinct periods of illness with an interval of well being.

Second Group—This period of well being is not present, but there is a sustained course of indisposition of varying intensity.

Third Group—All the signs point from the start to meningeal and nervous tissue involvement.

In the first two groups there develops a picture of general systemic infection from which the child appears to recover completely or in part, and then to receive a second blow directly upon the cerebro-spinal tract. Some of the cases in groups one and two recover without ever developing signs of meningeal involvement. They have fever with symptoms falling into three main categories: gastro-intestinal, tonsillar and upper respiratory passage inflammation and general malaise without localization of symptoms. Following then a remission of all symptoms in the first group or a varying duration of symptoms in the second group, one of two things occurs—the patient promptly gets well or sudden evidence of meningeal involvement appears from which may follow recovery or paralysis. There are so frequently found in families where a frank paralytic case occurs, other children who present the same initial symptoms as the paralyzed child, but who recover without meningeal symptoms, that one is led to suppose that these are examples of infection in which no penetration of the meninges occurred. The third group may be looked upon as examples of the malady in which the systemic stage has been overlooked because of its triviality. The violent picture of the nervous symptoms dominates and drives the memory of slight indisposition from the mother's mind.

Every physician should think of the possibility of poliomyelitis when called to see a sick child during the summer months. It is essentially a disease of the July to December period, and mostly during July, August and September. In the records of the Hospital for Sick Children for nine years, only five cases were admitted which occurred outside of this period. One in April, one in May and three in June. Now what is going to suggest this disease to the doctor when summer complaints are prevalent in his practice? In its early hours the clinical course of poliomyelitis resembles in general that of all the acute infectious diseases of childhood. There is fever with its attendant symptoms. Then, depending upon which set of organs is chiefly involved, we may have (and this is usually the most common form) disturbance of the gastro-intestinal tract simulating a simple summer diarrhoea. Vomiting is likewise frequent. But tonsillar and pharyngeal inflammation or upper respiratory tract symptoms are not uncommon. Both of these may be followed by drowsiness. These symptoms may be present at the

onset of any of the diseases with which the physician is meeting at this time of year. I believe that the points which will be of greatest assistance are:

First—To remember the possibility of the case being one of acute anterior poliomyelitis.

Second—The sudden onset. In a great many cases the parent can almost recall the hour of the day when the symptoms commenced.

Third—The spine sign. Test for pain and stiffness of the neck and back and resistance or pain on attempted flexion of these parts. There is a stiffening of the body which is protective, and may be carried to a position of moderate opisthotonos. This accounts for the fourth point, *i.e.*,

Fourth—A mingled look of apprehension and resentfulness which is quite unlike the alert, bright and shining eye of other fevers; and regarding the eye, the sclera and cornea present a glazed porcelain-like appearance.

Fifth—Pain and tenderness in the muscles. This has often led to the disease being mistaken for rheumatism.

Up to this stage, in a great number of cases, there is no definite sign of involvement of the central nervous system. Of course there are others which present perfectly definite signs of nervous involvement almost at the beginning. When does meningeal involvement occur? It may be indicated by sudden and definite increase in the spine sign, rapidly developing headache or disturbance of tendon reflexes. Spinal fluid examination, however, has shown that meningeal reaction may be actively under way when there is no sign or symptom to indicate it.

To await a confirmatory paralysis is not now permissible. The spinal fluid alone presents absolute evidence that meningeal invasion has occurred. In view of the importance of giving serum early, preferably while it is still in the general systemic phase, multiple lumbar punctures if necessary should be done.

Regarding the more general signs and symptoms and course, one should mention that in association with these symptoms there appears sometimes very early, sometimes later, headache, drowsiness and irritability. This irritability is frequently manifested upon approaching the bed. He fears movement of his painful limbs. The reflexes are present early, and may even be exaggerated if there is much meningeal irritation. Decrease in the reflex is a sign of oncoming paralysis, and of course absence occurs in the paralyzed muscle groups. Diarrhoea is a common symptom during the systemic phase, but one of the most striking facts in the whole disease is the almost universal occurrence of constipation during the second phase. The temperature curve is frequently of short duration, and falls rapidly through 24 to 48 hours. Not infrequently, however, irregular or prolonged curves are met with.

During the very earliest stages the cerebro-spinal fluid is practically negative. There may be a slight increase in globulin. The pressure and volume are, however, practically always increased. Soon after the onset of paralysis, our usual findings at the Hospital for Sick Children have been that the fluid is clear, under considerable increase of pressure, with a slight increase in globulin and a cell count of 12 to 300. Draper quotes counts reaching to 2,500 cells per c.m.m., and states that fluids

showing less than 100 cells in the first 12 to 18 hours following signs of meningeal invasion, are not likely to develop paralysis. The lymphocytes are usually high in preponderance, but very early there may be a preponderance of polymorphonuclears. Out of 111 cases which Dr. Park reviewed at the Hospital for Sick Children, one case revealed 315 cells, another 255 cells. 11 cases were between 100 and 200, and the remainder below 100. The globulin tended to increase as the cells decreased, and remained present for long periods when the fluid was otherwise normal.

The length of time between the first symptoms and the paralysis varies.

Dr. Park in reviewing the records of the Hospital for Sick Children found:

Less than 1 day	1 day	2 dys	3 dys	4 dys	5 dys	6 dys	7 dys	8 dys	not stated	no paralysis
5	2	10	6	4	7	2	2	1	4	4

When complete recovery occurs, it usually does so rapidly in from four to six weeks of the onset. During this second stage the affected muscles begin to waste and contractions begin to occur. Vasomotor phenomena, such as coldness and blueness of the extremities, also make their appearance. I should like to especially mention, however, the tendency to a marked neuritis which frequently occurs soon after the temperature has dropped to normal. This neuritis was particularly prevalent in the cases which have occurred in Toronto during the past summer. It has been most marked in the sciatic and femoral nerves of the affected limb, and marked tenderness is present along the course of these nerves. It is severe, and may keep the child awake crying with pain all night. Improvement in muscles may extend even over several years.

Regarding the prognosis—death in uncomplicated cases almost invariably results from failure of the muscles of respiration. If these are not affected the chance for life is good. As a rule the profoundly stuporous cases get well. Increasing apprehension and alertness with an existing paralysis is of grave significance. As mentioned, Drayton thinks that cell counts under 100 during the first 12 to 18 hours are not likely to develop paralysis. Regarding the paralysis itself, it is remarkable the recovery that takes place in the badly paralyzed muscles, and partial cripplings frequently fully recover. Even after long periods unlooked for improvements may occur.

The results of treatment with human convalescent serum recorded by Draper, Amos and Taylor have been very encouraging. The important point is that it be given early. If given before paralysis occurs, it is believed that it will prevent the extension of the inflammation into the cord or brain and so prevent paralysis or possibly death. If it is not possible to diagnose the case at this stage, frequent lumbar punctures should be done and the serum given as soon as the spinal fluid shows the presence of globulin and an increase in cells. Patients with fever presenting the picture of headache, drowsiness and irritability, should be punctured. It usually has a sedative effect as well as giving early information of such importance. The usual custom is to give the serum

into the spinal canal in not more than 15 c.c. doses after an equal or greater amount of the cerebro-spinal fluid has been withdrawn. Also it should be still more effectual if given intravenously. The most potent serum is that recovered from individuals who have recovered 3 to 4 months previously. Rosenow has reported brilliant results from the use of his anti-poliomyelitis streptococcus serum. If convalescent serum cannot be obtained, it would be wise to use this.

Regarding the subsequent treatment I shall only treat on general lines. Rest is essential. Paralyzed or weak muscles should be rested in the position of least stretching, and to protect them from the over-action of their unparalyzed opponents, splints will usually be necessary. Passive movements and massage should not be employed until all tenderness has disappeared, and then only by experts. The taking of weight on weakened leg muscles should be forbidden for several months. The parents should be warned at the outset that in order to get the maximum return of power it will require months of treatment, and that they will have a constant bombardment from friends and relatives to forsake the straight and narrow paths of orthodox treatment by regulars and stray into the alluring bypaths of the irregulars. It is our duty, however, to keep them out of such hands, and if we do so even in desperate cases it is wonderful the improvement which will often occur.

SOME CLINICAL ASPECTS OF THE NEWER WORK ON CARBOHYDRATE METABOLISM—LIVER FUNCTION

Samuel Soskin, '26.

In presenting these considerations on the clinical aspect of the newer work on carbohydrate metabolism, I shall not attempt either to further substantiate or disprove the theories previously formulated. Assuming that the proofs which have been offered are sufficiently sound, I shall merely try to present the physiology of the liver, in the light of recent work, and the relation of these new ideas to our conception of a few relevant clinical conditions. I shall endeavour to point out wherein this new work accords with our present knowledge of those conditions, and affords us a more rational conception of their etiology.

Statistics from the work of reliable investigators have more or less proven:—

(1) That carbohydrate, and carbohydrate only, is burned during muscular exercise. Hence it follows that, since the diabetic must expend some muscular energy, he must be able to burn carbohydrate.

(2) That fat, before being burned in the body, is converted into glucose.

(3) That glycogen is a specific secretory product of the hepatic cells, one source of materials for glyconeogenesis in the liver being fat.

Any discussion on the mechanism of carbohydrate metabolism, in the living organism, must take account of three main factors—the liver, the

pancreas, and the muscles. The metabolic processes in muscular activity have been earnestly investigated by Meyerhof and the Cambridge school of research. A great deal of light has been shed upon the physiology of the pancreas by the recent work on diabetes and insulin, at Toronto. But the liver, perhaps the most important of this triad, has for some reason been overlooked, and the knowledge of its physiology, until very recently, has been neglected.

The liver has five functions:—

(1) It manufactures and excretes blood-sugar.

(2) It forms urea from the waste nitrogen of the body.

(3) It de-aminates amino-acids.

(4) It destroys uric acid.

(5) It makes and excretes bile pigment.

And of these five, the production of blood-sugar and the supplying of this product to the body, is probably its most urgent function.

The work of Mann, of the Mayo Clinic, on total and subtotal hepatectomy in dogs, has done much to lighten the obscurity surrounding liver function.

Total hepatectomy in dogs is invariably fatal within 35 hours, the adrenal cortex being perhaps the only other secretory organ as necessary to life as the liver. When such an operation is performed:—

(1) There is a rapid and progressive fall in the level of the blood-sugar. It has been found that, to keep the blood-sugar of a totally de-hepatized dog at its normal level, requires the intra-venous injection of ½ gram glucose, per Kilo. body weight, every two hours. And, it is important to note, this same quantity of glucose injection is required by a dog which has been de-pancreatized previous to the removal of its liver.

(2) Total hepatectomy is also followed by a sharp fall in the urea content of the blood and urine, the waste nitrogen being excreted in the form of ammonia, which is correspondingly increased in amount.

(3) After removal of the liver, amino-acids appear in the urine.

(4) The enormous increase of uric acid in the blood and urine, is a striking feature of the sequelae of total hepatectomy. In such an experiment, the uric acid which separates out and settles from the urine, on standing, may not uncommonly occupy half the volume of the urine. Here, in passing, it is interesting to note the relation of these facts to gout. Attention, in gout, has chiefly tended to be focussed on the ability of the kidneys to excrete uric acid. The facts under discussion must make it apparent, however, that the problem of gout is primarily concerned with the ability of the liver to destroy uric acid. It is also worthy of note, that the level of uric acid in the blood, in the absence of kidney lesion, may be used as a test for hepatic function.

(5) Finally, total hepatectomy is followed by jaundice. Direct and indirect van den Bergh tests are given by the blood; and it has been shown, in the course of this work, that the amount of bile pigment production for which the liver is responsible is approximately 50% of the total amount arising in the body.

When a subtotal hepatectomy is done, *i.e.*, when only part of the liver is removed, there occurs:—

(1) A fall in the blood-sugar level.

(2) Some decrease in the urea excretion, and increase in the ammonia excretion.

(3) The appearance of amino-acids in the urine.

(4) A rise in the uric acid content of the blood and urine.

(5) Jaundice may or may not appear.

In short, all the sequelae of a total hepatectomy may be observed, but to a lesser degree.

In the pursuit of this work on partial removal of the liver, some very interesting facts have been discovered in regard to the ability of the liver cords to regenerate. It has, of course, long been known that autopsy may reveal microscopic evidence of parenchymal regeneration in the liver, in cases having a previous history of hepatic disease. But it has only recently been shown by Mann, whose work on hepatectomy represents some of the most highly developed technical skill in experimental surgery, that after successful removal of half the liver, one may, within 24 hours, find the liver tissue regenerated to its original volume. So much so is this the case that, in order to make certain, for experimental purposes, that only a small volume of the liver is functioning, it has been found necessary to discourage regeneration, by diverting the portal blood supply of the liver into the Inferior Vena Cava, by an Eck fistula.

Having discussed the normal functions of the liver, and noted the effect of experimental diminution of those activities, let us now see what relation these observations bear to the known facts of some few clinical conditions, in which liver damage is the chief item in the pathological picture.

Acute Yellow Atrophy is such a condition. It is defined (Delafield & Prudden) as "An acute, widespread, autolytic necrosis of the liver cells, of unknown origin, characterized by jaundice, toxaemia and a reduction in the volume of the liver." At autopsy, the liver is found to be small, flabby, and with a wrinkled capsule. Microscopically, the centres of the liver lobules are seen to be necrotic. These necrotic areas are surrounded by a zone of so-called "fatty degeneration", while about this again is a shell of normal hepatic tissue. Such a liver picture may be found associated with a variety of clinical diagnoses, among which are:—Typhoid fever, diphtheria, puerperal infection, eclampsia, and pernicious vomiting of pregnancy.

The signs and symptoms in Acute Yellow Atrophy include headache, delirium, muscle tremor, sometimes convulsions, haemorrhage into the skin and mucous membranes, vomiting, and jaundice. These signs and symptoms, however, which vary in order of prominence with the associated clinical condition, do not concern us so much as do the laboratory findings. The latter reveal:—

(1) An increase in the ammonia excretion of the urine, from the normal 2-5% up to 17% (Herter), and a corresponding decrease in the

urea excretion. (Part of the increased ammonia output can be accounted for by an increased demand for alkali, due to the acidosis which usually occurs.)

(2) The presence of amino-acids, notably leucin and tyrosin, in the urine. Hunter, in 23 collected cases, found only 9 which did not show the presence of either leucin, tyrosin, or both.

(3) An increased uric acid content of the blood and urine.

(4) An increased bile pigment of the blood, as evidenced by the van den Bergh reaction, the presence of bile in the urine, and the appearance of jaundice.

(5) A lowered blood-sugar. In regard to this there is not an abundance of data, due to the fact that it is only comparatively recently that records of hypoglycaemia have become available, previous records showing only variations in blood-sugar above the normal. Older records do show an occasional hyperglycaemia in acute yellow atrophy, which, when it occurs, we can regard as a transient result of liver irritation early in the disease, when, as in diabetes, the liver does not seem able to retain its glycogen stores.

If we now turn to other conditions, in which the liver injury that occurs is of known etiology, we find data quite parallel to that in Acute Yellow Atrophy.

In chloroform, salvarsan and phosphorus poisoning we find a similar fall in blood-sugar, increase in ammonia and decrease in urea excretion, presence of amino-acids in the urine, increased uric acid in the blood and urine, and evidence of increased bile pigment in the blood. Just as the signs and symptoms vary in order of prominence with the particular toxic agent involved, so do the laboratory findings. For example, chloroform and phosphorus are particularly apt to maim the blood-sugar production in the liver, while salvarsan is inclined to spare it. However, in all, there is an increased total nitrogen output, and in all, if nitrogen equilibrium is maintained, it is maintained only when there is an increased ingestion of carbohydrate. (Lusk.) This, of course, we can ascribe to failure of the damaged liver to maintain an adequate supply of blood-sugar, from other than carbohydrate sources. In this connection, it is very interesting to note the recent prophylactic measure adopted against chloroform poisoning. The administration of carbohydrates to patients, previous to their subjection to chloroform anaesthesia, is a splendid example of a more or less empirical measure being later justified in theory, when the underlying principles have been laid bare. This work also confirms the advisability of the use of high carbohydrate diets in the conditions under consideration, among which is the pernicious vomiting of pregnancy, recently brought into prominence by the investigations of Professor Harding of this University.

A constant feature of these conditions of liver damage due to toxic agents, known or unknown, is the fatty condition of the liver, commonly known as "fatty degeneration". In such conditions, Virchow assumed a fatty degeneration of protein, in which the tissue protein was converted into fat, as distinguished from a fatty infiltration, in which body fat passed into the liver cells. This idea of fatty degeneration of protein

in the old sense, which has obtained such a strong hold on pathologists, has been largely disproven by the work of Rosenfeld, who has shown that, in general, such collections of fat are the result of transference of fat from the fat depots of the body. We are therefore justified in assuming that the fatty condition of the liver, in the hepatic disorders under discussion, is the result of an accumulation of blood-borne fat, due to the inability of the liver to utilize it for the production of carbohydrate.

The clinical entities we have thus far touched upon have been characterized by hepatic disorder. Let us now briefly consider the phenomena observed in starvation, where the liver is not at fault, but where the food intake of the body has ceased, and therefore the food supply to the liver altered.

We know that, in starvation, the body, failing to receive its fuel supply from extraneous sources, first utilizes its available carbohydrate, then depletes its fat stores, and finally consumes itself by utilization of its own tissue protein, as a source of fuel supply.

In the first days of fasting, the amount of protein metabolized depends upon two factors:—

(1) The glycogen content of the individual.

(2) The quantity of protein ingested before the starvation period.

The use of stored glycogen in the body has been shown to spare the body protein for about the first day of fasting. By the fifth day, the previously ingested protein has been eliminated as a factor in protein metabolism, and the urea excretion has reached a more or less constant level. In order to maintain nutrition, it has been shown that protein, from muscle and other tissues, now passes into the blood and is carried to all organs for the nutrition of their cells.

It is a well-established fact that fat animals can fast for longer periods than lean ones. (This is complicated by the occurrence of acidosis in man.) Folin and Denis, among others, have shown that protein metabolism is low, when ample fat is present, and that the total quantity of protein metabolism which occurs in starvation depends upon the amount of fat originally present in the body.

In spite of the fact that the carbohydrate stores of the body are first to be utilized in the effort to save the body protein, the liver, in starvation, is never free of glycogen. Furthermore, it has been shown that if the liver in a fasting animal is rendered free of glycogen, which can only be accomplished by the use of cold and strychnine tetanus, glycogen soon reappears in the liver.

With the above observations in mind, it seems reasonable to assume that the lipaemia and fatty condition of the liver, which occur in starvation, are evidences of an increased migration of fat from the fat depots of the body to the liver, in order that the latter may have sufficient raw materials for the manufacture and excretion of as much carbohydrate as possible, with which to supply the demand of the body tissues for fuel. This view of the process makes it very easy to explain the constant residue of glycogen in the liver, during starvation, and

its re-appearance if removed. The respiratory quotient of 0.72 in starvation points to fat as the chief metabolite, but does not preclude the possibility of the fat being first transformed into carbohydrate. The low nitrogen excretion, and especially the maintained blood-sugar, are also accounted for.

From these brief considerations, we may therefore conclude that the newer work on carbohydrate metabolism, especially as regards the specific secretion of blood-sugar by the liver, and the utilization of fat in that process, is in remarkable accord with our clinical and laboratory experience of diseases associated with liver damage and with our knowledge of starvation phenomena. It also confirms the value of some therapeutic measures, to which we have alluded.

FACULTY NOTES

Medical Society

The Second Annual Dinner of the Medical Society was held in the Great Hall of Hart House on Friday evening, February 19th, 1926. The Vice-President of the Medical Society, Mr. K. E. Ferrie, acted as toast master of the evening. Dean Primrose, Prof. J. P. McMurrich and Prof. J. J. R. Macleod replied to the toasts for the occasion—proposed in turn by Mr. C. H. Rutherford, Mr. D. H. Marritt and Mr. O. A. Kilpatrick.

The occasion was honoured by the presence of a very distinguished guest in the person of President Wilbur of Leland Stanford University, California.

The presentation of trophies to the Water Polo, Rugby and Track teams, winners of their respective Interfaculty Championships, and the awards for the various inter-year events was an item of interest.

The results of the undergraduate elections for 1926-27 were announced during the evening.

The committee in charge of the dinner were K. E. Ferrie, H. D. Marritt, G. D. Wilson, and J. M. Maxwell.

Mr. J. F. Dreyer represented the Medical Society at the School of Science At-Home at the King Edward Hotel on March 5th.

Mr. B. B. Sparks represented the Medical Society at the Annual Dental At-Home held in the Pompeian Room at the King Edward Hotel on Tuesday, February 16th.

Medical Athletic Society

The Indoor Track team have made a splendid showing this year, and in a close contest lost by a very few points to School of Science. Medicine was unfortunate in not having a greater number of men competing. The brunt of the meet was borne by "Mo" Mitchell, that versatile runner, who alone scored twenty points for Medicine. He won the 220 yard and 440 yard dash, as well as the half-mile, together with occasional points in other events.

Medicine has lost the only championship which was won last year. The greater number of entries by the Ontario College of Agriculture

brought for them a sufficient number of points to win the cup. However, those men in Medicine who did enter this year did well.

In Boxing, Ken Fidler and Robertson won their bouts. Harry Hill put up a splendid fight against Joe Mahon, for many years Intercollegiate heavyweight champion.

In Wrestling, Danny Webster and Ed. Long each won his bout.

These men greatly assisted Varsity in winning once again the Intercollegiate Assault-at-Arms.

Unfortunately all Medical Hockey and Basketball teams, although apparently strong at first, have been eliminated.

So the athletic year closes with three trophies to the credit of Medicine, the Mulock Cup, Rowell Memorial Cup and Echardt Cup. The last two have not previously been won by Medicine for a number of years.

Junior Medical At-Home

Hart House was the scene of the Junior Medical At-Home on the evening of Friday, February 26th, under the patronage of Mrs. A. Primrose, Mrs. E. Stanley Ryerson, and Mrs. A. Hunter. The East Common Room and the lower gallery were delightfully decorated with coloured lights and palms. Excellent music, gay streamers and novelties, together with a tasteful lunch in the Great Hall, combined to make a very pleasureable evening.

The Committee comprised G. E. D. Wilson and D. R. Hillery of 2T9, N. L. Murray and H. R. Inksater of 3T0, B. P. Sparks and A. R. Benson of 3T1.

Research

By special request of the Rockefeller Foundation, Prof. Klotz of the Department of Pathology and Bacteriology of this University is leaving on May 1st next for Lagos, West Africa, where for six months he will investigate the various aspects of Yellow Fever in that country. The University of Toronto is greatly honoured in the choice of Dr. Klotz for this work.

New Clinical Building

In the reply to the toast to the Faculty at the Annual Medical Society Dinner at Hart House, Dean Primrose announced the plans for the new building which is to accommodate the Clinical Departments of Medicine, Surgery and Obstetrics, and Gynaecology of Toronto General Hospital. These plans also make provision for the Banting and Best Chair of Medical Research.

This announcement is the fulfilment of the hope of many members of the staff, and affords a further aid to a more scientific practice of medicine.

"Sunshine" Hospital

A representative group of Toronto's business and professional men were the guests of Sir Wm. Mulock at the York Club on the evening of February 23rd, and warmly endorsed the plans for a new Convalescent Hospital for Sick Children. The building will be erected at Thistletown.

Dr. W. E. Gallie and Dr. Alan Brown addressed the group, and pointed out the imperative need for such a hospital. Plans are well under way for the successful completion of the project, which will have the hearty support of both the laity and the profession.

Student Christian Association

On Thursday, January 28th, Prof. J. P. McMurrich addressed a large and intensely interested group of students on the subject "The Grounds of an Evolutionist's Faith." During the course of his address Prof. McMurrich pointed out that the Bible was written by man at an age when little was known about science, and hence could not be expected to give a sound opinion on scientific problems. However valuable the Bible is, it is not the only revelation of God. The thoughtful man sees God in nature. The scientist as he delves into the origin of things comes ultimately to God. Prof. McMurrich urged the students to keep on thinking, and pointed out that religion is a personal thing which has to be determined by each man individually.

Daffydil

The annual gala of staff and students of the Medical Faculty which was held in Convocation Hall on February 11th and 12th, proved to be one of the outstanding events of the year.

The year skits offered a happy combination of wit and dramatic finish and showed much careful preparation. The skit presented by the ladies was artistically done and very worthy of mention.

For the past three years the cup has been successively, and so permanently, won by 2T6. The graduating year have, however, re-presented it for competition and this year it was awarded by the judges to 2T8 for the best skit of the evening.

The impersonation of the various members of the staff was generally enjoyed because of its customary "personal touch."

The several committees in charge are to be congratulated on the production.

The Annual Medical Society Dinner

The annual elections of the Medical Society, together with election of the permanent executive for the graduating year and the executive bodies for the undergraduate years took place in the Medical Building on Friday, February 19th. The results were as follows:

Medical Society Executive: *President,* G. H. Rutherford; *Vice-President,* O. A. Kilpatrick; *Secy-Treasurer,* J. A. Fallon; *Assistant Secy-Treasurer,* J. Lind.

Medical Athletic Association: *President,* H. D. Marritt; *Vice-President,* L. M. Mullen; *Secy-Treasurer,* R. M. Mitchell; *3T0 Representative,* W. A. Monkhouse; *3T1 Representative,* R. E. Morgan.

Permanent Executive 2T6: *President,* N. A. McCormick; *Vice-President,* C. R. Weber; *Secy-Treasurer,* J. C. Goodwin; *Hon. Secretary,* Miss E. M. Fleming.

Year Executive 2T7: *President,* D. A. Macklin; *Vice-President,* W. T. MacNicoll; *Secretary,* Miss A. M. Hilliard; *Treasurer,* F. D.

Linton; *S.A.C. Representative,* J. B. Laidlaw; *S.C.A. Representative,* W. E. Park; *Varsity Representative,* J. R. Westheimer.

YEAR EXECUTIVE 2T8: *President,* D. M. Campbell; *Vice-President,* K. G. Gray; *Secretary,* Miss M. F. Thompson; *Treasurer,* J. G. Shannon; *S.A.C. Representative,* R. F. Brown; *S.C.A. Representative,* H. F. P. Grafton; *Varsity Reporter,* F. S. Leeder.

YEAR EXECUTIVE 2T9: *President,* O. L. Stanton; *Vice-President,* S. V. Railton; *Secretary,* Miss M. Grant; *Treasurer,* H. A. Ansley; *S.A.C. Representative,* C. E. D. Wilson; *S.C.A. Representative,* H. G. Miller; *Varsity Reporter,* A. H. Walker.

YEAR EXECUTIVE 3T0: *President,* J. E. Long; *Vice-President,* W. S. Kergin; *Secretary,* Miss M. K. Patterson; *Treasurer,* W. W. D. Williams; *S.A.C. Representative,* M. L. Murray; *Varsity Reporter,* J. L. Blaisdell.

YEAR EXECUTIVE 3T1: *President,* H. Ebbs; *Vice-President,* J. M. Spence; *Secretary,* Miss A. M. Walters; *Treasurer,* B. B. Sparks; *S.A.C. Representative,* D. B. Smith.

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